REMARKS

Reconsideration is requested.

Claims 48-64 are pending. Claims 58-64 have been added. Support for the new claims and amended claims may be found throughout the specification. No new matter has been added. Specifically, claims 58 is similar to unamended claim 49. Claims 48 and 49 have been added based on, for example, the disclosure of pages 6 and 7 of the specification. Claims 59-64 have been added to define further patentable embodiments of the disclosed invention.

The Examiner is again urged to appreciate that the application describes the claimed inhibitor as being, for example, an alkaline protein, having a molecular weight of 40-43 kDa and pI of greater than about 7.0 at, for example, page 5, lines 23-31, and page 19, lines 25-30 of the specification, as well as originally-filed claims 14 and 15. The recitation of dependent claims 50, 59 and 60 is described, for example, at page 5, line 31 to page 6, line 3, page 6, lines 11-16, page 20, lines 5-8 and originally-filed claims 8-12 of the specification.

The recitation of dependent claims 51 and 61 is described, for example, at page 6, lines 3-10, page 6, lines 17-28, page 20, lines 9-16 and originally-filed claims 8-12 of the specification. The recitations of dependent claims 52-57 and 62-64 are described, for example, at page 5, lines 14-23.

The specification describes the claimed inhibitor as resolving in to two protein bands following reduction with ß-mercaptoethanol. Specifically, the application includes the following description of the claimed inhibitor:

> "a proteinaceous species having a pI ... of greater than about 7.0 ... [and having] ... a molecular weight as determined by SDS-page [which] is typically 40-43 kDa. Following reduction with ß-mercaptoethanol three SDS-page protein bands are found with SDS-page molecular weights of ca. 40-43 kDa, ca. 30 kDa, and ca. 10 kDa. See, page 5, lines 24-31 of the specification.
>
> In this way, we obtained a fraction (1 mL) of the inhibitor which migrated as a single protein band on SDS-PAGE. It had an apparent molecular weight of ca.[1].40-43 kDa. Following reduction with ß-mercaptoethanol, two additional SDS-PAGE bands of molecular weights of typically 30 and 10 kDa are detected. See, page 19, lines 24-30 of the specification.
>
> [Originally-filed claim] 14. Inhibitor as in any of claims 7 to 13, characterised in that said protein or glycoprotein is selected from the group comprising proteins or glycoproteins having a molecular weight typically between 40 kDa and 43 kDa, proteins or glycoproteins having a molecular weight typically 30 kDa and proteins or glycoproteins having a molecular weight of typically 10 kDa.

The specification does not describe the inhibitor as containing two subunits.

The Examiner as repeatedly stated that the specification "describes a xylanase inhibitor which is a ... protein having two subunits ..." (see, page 2 of Paper No.18, and page 2 of Paper No. 11) and that the specification is "enabling for xylanase inhibitor which is a ... protein having two subunits..." (see, page 3 of Paper No.18, page 2 of Paper No. 14 and page 3 of Paper No. 11).

The Examiner has indicated that amending the claims to recite, in part, that the claimed inhibitor "is a ... protein having two subunits with an amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2,..." would be helpful in overcoming the outstanding Section 112, first paragraph, "written description" (see, page 3 of Paper No. 18), and presumably also the "enablement", rejections of claims 48-57.

The applicants respectfully submit however that such a recitation, as is suggested by the Examiner, would not be appropriate as the same is not believed to be supported by the specification. As has been explained in the Amendment of December 17, 2002, and above, the specification teaches that the inhibitor of the claimed invention is, among other things, a protein or glycoprotein which migrated as a single protein band on SDS-PAGE, having an apparent molecular weight of ca. 40-43 kDa. Following reduction with ß-mercaptoethanol, two additional SDS-PAGE bands of molecular weights of typically 30 and 10 kDa were detected. The specification does not describe these separate bands as "subunits" as characterized by the Examiner. The applicants submit, with due respect, that to so characterize the presently disclosed invention is inappropriate.

Moreover, the Examiner's suggestion that the claims define the invention as being a protein "having two subunits with an amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2" appears to be unclear as the applicants do not believe the specification describes two subunits wherein each subunit has an amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2, as suggested by the Examiner.

The applicants have previously presented the above concerns to the Examiner in the Amendment of December 17, 2002, which the Examiner indicates have been "fully considered" (see, page 2 of Paper No. 18) and yet the Examiner's comments of Paper No. 18 fail to address any of the applicants previously presented and above-repeated concerns.

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[1] "ca. ... circa" and "circa ... In approximately" See, pages 1344 and 264 of WEBSTER'S II New Riverside University Dictionary, The Riverside Publishing Company, A HOUGHTON MIFFLIN COMPANY, Boston MA (1984).

The pending claims define the disclosed inhibitor most broadly by independent claims 48, 49 and 58. Each of these claims defines the claimed inhibitor as being an isolated proteinic or glycoproteinic inhibitor of xylanase, which is a water-soluble, alkaline protein or glycoprotein, has a pI of greater than about 7.0 and has a molecular weight of about 40-43 kDa as measured by SDS-PAGE. (Claims 48 and 49 further define the inhibitor as containing an N-terminal amino acid sequence which is at least 70% homologous to SEQ ID NO:1, which will be further discussed below.)

Claims 49 and 50 further define the inhibitor as resolving as two separate bands on SDS-PAGE after reduction with ß-mercaptoethanol, said two separate bands having molecular weights of about 30 kDa and about 10 kDa. This feature of the claimed invention is a further characterization however which should not be required to define the invention described and enabled by the specification. One of ordinary skill in the art will recognize, from at least the passages noted above, that the applicants were in possession of the claimed invention at the time the application was filed (i.e., the specification describes the claimed invention). Moreover, one of ordinary skill would be able to make and use the claimed invention from the present description.

Specifically, the present specification teaches that the claimed inhibitors are present in both barley (BWM) and rye (RF) (see page 20, line 18 to page 21, line 24, and in particular to line 1 of page 21, of the specification). Thus, the present invention not only teaches for the first time the fact that proteinaceous xylanase inhibitors are present in plants (and in particular cereals), but also teaches the isolation of such an inhibitor from wheat and characterization of same, including providing the N-terminal amino acid sequence of this inhibitor, i.e. SEQ ID NO: 1. The present specification

further teaches that the claimed inhibitors are obtainable from, for example, rye and barley and specifically teaches that extracts of these cereals clearly demonstrate xylanase inhibition.

As an example, the applicants note that the specification describes and the applicants have claimed inhibitors obtainable from barley. Such an inhibitor is specifically disclosed in WO01/98747 (copy attached and listed on the attached PTO 1449 Form), the U.S. national phase of which has been assigned U.S. Serial No. 10/311,886. The barley inhibitor (designated HvXI) specifically described therein comprises an amino acid which is 78.6% homologous[2] with that of SEQ ID NO:1 of the present application.

The identification of the barley sequence therefore serves as evidence that a further, albeit separately patentable, species of the presently claimed genus or subgenus exists, as described and enabled by the present specification. Moreover, with specific regard to the claimed recitation of the claimed inhibitor having an N-terminal amino acid sequence which is at least 70% homologous to SEQ ID NO:1, the barley sequence serves as evidence that a xylanase inhibitor, as claimed, having an N-terminal amino acid sequence which is at least 70% homologous to SEQ ID NO:1, was

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[2] Homology calculated using:
http://searchlauncher.bcm.tmc.edu/seq-search/alignment.html
Results of SIM with:
Sequence 1: HvXI 30, KALPVLAPVTKDAATSLVTI (20 residues)
Sequence 2: TAXI 30N, KGLPVLAPVTKXTA (14 residues (SEQ ID NO:1 of present applciation)
using the parameters:
Comparison matrix: BLOSUM62
Number of alignments computed: 20
Gap open penalty: 12
Gap extension penalty: 4
78.6% identity in 14 residues overlap; Score: 52.0; Gap frequency: 0.0%
HvXI 30, 1 KALPVLAPVTKDAA
TAXI 30N, 1 KGLPVLAPVTKXTA

described and enabled by the present specification and has been identified by a skilled person following the teachings of the present specification.

With further regard to the enablement and written description support of the recitation relating to the recited homology of the N-terminal sequence of the claimed inhibitor to SEQ ID NO:1, the Examiner is requested to consider the following.

SEQ ID NO:1 is 14 amino acids in length. One of ordinary skill in the art will appreciate that the specification describes an N-terminal amino acid sequence which is at least 70% homologous to SEQ ID NO:1. Moreover, the description of the barley species in the above-identified application is compelling evidence that the present specification is enabling for inhibitors with the claimed structural and functional properties, including the presence of an N-terminal sequence having greater than 70% homology with SEQ ID NO:1 of the present application.

It is well-known in the present art to describe protein sequences by a relative percent homology or identity to a base sequence. Such descriptions, and the desire for a simple means to make such calculations, led to the development and ready availability of, for example, the BESTFIT program.[3]

The U.S. Patent Office has granted 7 patents wherein the term "percent homology" is recited in a claim in the biotechnology area. Moreover, the Patent Office

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[3] The attached Appendix A provides a list of the first 500 of 892 U.S. Patents issued from 1976 to a recent search which include the words BESTFIT and protein as an indication of the prevalence of the terms in the field of biotechnology. Each of the listed patents has not been reviewed in detail to assure the context in the listed patent is the same as used in the claims which are the subject of the present appeal. See, Appendix B for a description of the BESTFIT program.

has granted at least 20 patents wherein the term BESTFIT is recited as an example of calculation of the identity or homology in the biotechnology area.[4]

The present specification provides a functional and a structural description of the claimed inhibitors. The structural similarity of the proteins of the present claims, which reference a percent homology and a base comparison sequence, will be appreciated by one of ordinary skill in the art and has been recognized by the Patent Office (see, attached noted appendices) as providing an adequate written description of amino acid sequences.

The Patent Office's "current understanding... regarding the written description requirement of 35 U.S.C. 112, ¶1" (see, 66 FR 1099, Friday, January 5, 2001 (copy attached as Appendix D) states that

> "An applicant may show possession of an invention by disclosure of drawings[39] or structural chemical formulas[40] that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. The description need only describe in detail that which is new or not conventional.[41] This is equally true whether the claimed invention is directed to a product or a process.
>
> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well-known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of

[4]The attached Appendix C provides a list of the noted 27 patents, representative claims of each patent with the noted recitation and, in italics, the description of the relevant portions of the specification of each listed patent which describes the use of percent homology or the BESTFIT program as being routine. Many of these patents were granted to Human Genome Sciences and contain the same or very similar, limited "boiler plate" text which is repeated in multiple applications.

the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]" Id. at 1106.

The indicated footnotes 39-46 further support this "understanding" of the Patent Office based on Federal Circuit, CCPA and other case law as follows:

[39]*See, e.g., Vas-Cath*, 935 F.2d at 1565, 19 USPQ2d at 1118 ("drawings alone may provide a 'written description' of an invention as required by § 112"); *In re Wolfensperger*, 302 F.2d 950, 133 USPQ 537 (CCPA 1962) (the drawings of applicant's specification provided sufficient written descriptive support for the claim limitation at issue); *Autogiro Co. of America v. United States*, 384 F.2d 391, 398, 155 USPQ 697, 703 (Ct. Cl. 1967) ("In those instances where a visual representation can flesh out words, drawings may be used in the same manner and with the same limitations as the specification.").

[40]*See e.g., Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.").

[41]*See Hybritech v. Monoclonal Antibodies*, 802 F.2d at 1384, 231 USPQ at 94; *Fonar Corp. v. General Electric Co.*, 107 F.3d at 1549, 41 USP!2d at 1805 (source code description not required).

[42]For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been isolated. One skilled in the art may be able to determine when the gene disclosed is the same as or different from a gene isolated by another by comparing the restriction enzyme map. In contrast, evidence that the gene could be digested with a nuclease would not normally represent a relevant characteristic since any gene would be digested with a nuclease. Similarly, isolation of an mRNA and its expression to produce the protein of interest is strong evidence of possession of an mRNA for the protein.

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, unique cleavage by particular enzymes,

isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using" such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention").

[43]A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. *See also Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)).

[44]If a claim limitation invokes 35 U.S.C. 112, ¶ 6, it must be interpreted to cover the corresponding structure, materials, or acts in the specification and "equivalents thereof." See 35 U.S.C. 112, ¶ 6. See also *B. Braun Medical, Inc. v. Abbott Lab.*, 124 F.3d 1419, 1424, 43 USPQ2d 1896, 1899 (Fed. Cir. 1997). In considering whether there is 35 U.S.C. 112, ¶ 1, support for a means- (or step) plus-function claim limitation, the examiner must consider not only the original disclosure contained in the summary and detailed description of the invention portions of the specification, but also the original claims, abstract, and drawings. A means- (or step-) plus-function claim limitation is adequately described under 35 U.S.C. 112, ¶ 1, if: (1) The written description adequately links or associates adequately described particular structure, material, or acts to the function recited in a means- (or step-) plus-function claim limitation; or (2) it is clear based on the facts of the application that one skilled in the art would have know what structure, material, or acts perform the function recited in a means- (or step-) plus- function limitation. Note also: A rejection under 35 U.S.C. 112, ¶ 2, "cannot stand where there is adequate description in the specification to satisfy 35 U.S.C. 112, first paragraph, regarding means-plus-function recitations that are not, per se, challenged for being unclear." *In re Noll*, 545 F.2d 141, 149, 191 USPQ 721, 727 (CCPA 1976). See *Supplemental Examination Guidelines for Determining the Applicability* of 35 U.S.C. 112, ¶ 6, 65 FR 38510, June 21, 2000.

[45]See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94.

[46]*See, e.g., Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (starting "the description need not be in *ipsis verbis* (i.e., "in the same words"] to be sufficient")." Id. at 1109-1110. (Emphasis added.)

As noted above in footnote 40, the Patent Office confirms that the court in *Eli Lilly* found that claims involving generic formula usually indicate with specificity what the generic claims encompass. The court confirmed that one of ordinary skill in the art can usually distinguish such a formula from others and can identify many of the species that the claims encompass. Given these facts, the *Eli Lilly* court concluded that "such a formula is normally an adequate written description." The Patent Office reliance on *Lockwood* above is also of particular relevance.

In the present application, the applicants have described, and recited in the claims, a protein or glycoprotein, which is an inhibitor of xylanase, which is water soluble, which is an alkaline protein or glycoprotein, which has a pI of greater than about 7.0, and which has a molecular weight of about 40-43 kDa as measured by SDS-PAGE. The claimed protein or glycoprotein is further described in the claims by reference to an N-terminal amino acid sequences and a percent identity which allows one of ordinary skill to distinguish the generic formula of the claims from other protein sequences. One of ordinary skill can identify many species that the claims encompass. Given the conclusions of the *Eli Lilly* court, the applicants respectfully submit that the generic formula of the claims and the specification provide an adequate written description.

The issue before the *Eli Lilly* court, which was not mentioned in the footnote of the Patent Office's "written description" analysis, was whether even more generic statements, "such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more," is an adequate' written description. See, 43 USPQ2d 1406 (emphasis added).

The *Eli Lilly* court found that such a generic recitation was not an adequate written description.

> "because it does not distinguish the claimed genus from others except by function. It does not specifically define any of the genes that fall within its definition. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. *See Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*)." Id.

As noted above, the claims of the present application recite a reference sequence and a percent identity, as well as a molecular weight and other distinguishing features which allow one of ordinary skill to distinguish the protein of the claimed invention from other proteins.

The applicants respectfully submit that the present specification demonstrates possession of the claimed invention by, for example, disclosure of reference sequence (i.e., SEQ ID NO: 1) and the distinguishing features coupled with the functional characteristics recited in the claims. An ordinarily skilled artisan would have understood that the applicants were in possession of the claimed invention at the time of filing.

Beyond the Patent Office "understanding" of the requirements of the Section 112, first paragraph, written description, requirement, as detailed above, the Patent Office has issued Training Materials

> "designed to aid PTO's patent examiners in applying the interim written description... guidelines in a uniform and consistent manner to promote the issuance of high quality patents. The training materials will also assist patent applicants in responding to the PTO when... written description issues are raised during the

examination of a patent application." See, Press Release #00-15, USPTO, March 1, 2000 (www.uspto.gov/web/offices/com/speeches/00-15.html) (copy attached as Appendix E).

The Written Description Training Materials

(http://www.uspto.gov/web/offices/pac/writtendesc.pdf) offer the following Example 14 "Product by Function":

> **"Example 14: Product by Function**
> **Specification:** The specification exemplifies a protein isolated from liver that catalyzes the reaction of **A→ B.** The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following:
> substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.
> **Claim:**
> A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A →B.
> **Analysis:**
> A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art. A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3.
> Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising". The claim has two different generic embodiments, the first being a

> protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.
> A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious. There is actual reduction to practice of the single disclosed species.
> The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
> **Conclusion:** The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

The claims at issue in the present application relate to a protein or glycoprotein inhibitor which may be obtainable from a cereal plant or fraction thereof, such as from wheat, rye, triticale, barley, sorghum, oats, maize and rice. The "catalytic activity" described in the above-quoted Example 14 may be seen as analogous to the functional recitations in the present claims, as noted above. Moreover, the present claims further describe the claimed inhibitor by reference to a characteristic molecular weight. The "SEQ ID NO: 3" of the above quoted Example 14, may be seen as analogous to the SEQ ID NO: 1 of the pending claims. Finally, the "variants of the protein" discussed in the above-quoted Example 14 exemplifies the proteins of the presently claimed invention which contain an N-terminal amino acid sequence with is at least 70% homologous to SEQ ID NO:1. As with the above-quoted Example 14, the applicants submit that

methods of making and identifying and testing proteins of the claimed genus are well know and would not require undue experimentation from the teachings of the specification and the generally advanced level of skill in the art.

The Patent Office's analysis and "understanding" of the "written description" requirements of 35 U.S.C. § 112, first paragraph, and assistance to examiners and applicants in applying the law, as expressed through the Training Materials, all support the applicants belief that the presently claimed invention is supported by an adequate written description.

Withdrawal of the 35 U.S.C. § 112, first paragraph, "written description" rejection of claims 48-57 is requested.

The 35 U.S.C. § 112, first paragraph, "enablement" rejection of claims 48-57should be withdrawn for many of the reasons noted above. Withdrawal of the rejection are requested in view of the above and the following further comments.

The applicants submit that the specification enables one of ordinary skill in the art to make and use the claimed invention. The Examiner is requested to see, for example, the above description and discussion regarding the applicants elucidation of the barley sequence.

The Examiner alleges that an undue amount of experimentation would be required to make the presently claimed invention based on the Examiner's belief that further species within the claimed genus could only be made by "screen[ing] a vast number of organisms for any proteinic or glycoproteinic having any structure or amino acid sequence with a pI of greater than 7.0 and a molecular weight of 40-43 kDa and determining whether the protein or glycoprotein is still able to inhibit xylanase enzyme

activity" (see, page 3 of Paper No. 18). The applicants respectfully submit however that to "screen" organisms does not require undue amounts of experimentation, especially in light of the methods exemplified in the present specification. While the amount of work may be extensive, depending on the number of "organisms" to be screened, the experimentation is routine. Moreover, the applicants respectfully submit that a "vast" number of organisms are not required to be screened. The applicants have described and claimed xylanase inhibitors from cereals, and specifically from wheat, rye, triticale, barley, sorghum, oats, maize and rice, such that further species within the claimed genus could be obtained by "screen[ing]" a relatively small number of "organisms". Finally, the applicants respectfully submit that it is just as likely that the ordinarily skilled person reading the present application would "screen" for xylanase inhibitor activity of protein and/or glycoprotein extracts and then identify or characterize the pI and molecular weight and N-terminal amino acid sequence, thereby reducing the uncertainty and amount of work required according to the Examiner's scenario (i.e., "and determining whether the protein or glycoprotein is still able to inhibit ..." (emphasis added)).

The present specification is submitted to provide more than adequate guidance for one of ordinary skill to make and use the claimed invention.

The above-described barley sequence and attached WO publication are evidence that a species within the genus of the present claims could be made from the description of the present application.

The present specification describes methods of extracting inhibitors of the claimed genus. See, pages 11-15 of the application. The application describes

methods of determining molecular weights and isoelectrofocusing. See, page 15 of the application. The present specification describes methods of determining the N-terminal amino acids sequence of proteins of the invention. See, page 15 of the present specification. The present application describes evidence of the presence of endoxylanase inhibitors in wheat. See, pages 16-20 of the specification. Finally, the specification exemplifies the use of a xylanase inhibitor of the invention. See, pages 20-21 of the specification. The specification therefore provides evidence of the ability of one of ordinary skill in the art to make and use the claimed invention.

Reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph, "enablement" rejection of claims 48-57 is requested.

The claims are submitted to be in condition or allowance and a Notice to that effect is requested.

The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

B. J. Sadoff
Reg. No. 36,663

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX A

List of first 500 of 892 U.S. Patent issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

APPENDIX A

List of first 500 of 892 U.S. Patents issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

1	6,506,962	Acquired resistance genes in plants
2	6,506,603	Shuffling polynucleotides by incomplete extension
3	6,506,602	Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
4	6,506,569	Antibodies to human tumor necrosis factor receptor TR10
5	6,506,565	Plant regulatory sequences for selective control of gene expression
6	6,506,559	Genetic inhibition by double-stranded RNA
7	6,504,084	Maize NPR1 polynucleotides and methods of use
8	6,504,083	Maize Gos-2 promoters
9	6,504,082	Ecdysone receptors and methods for their use
10	6,504,010	Compositions and methods for the therapy and diagnosis of lung cancer
11	6,504,009	Transcriptional regulator
12	6,503,744	Campylobacter glycosyltransferases for biosynthesis of gangliosides and ganglioside mimics
13	6,503,735	Polynucleotides encoding chemokine .beta.-15
14	6,503,729	Selected polynucleotide and polypeptide sequences of the methanogenic archaeon, methanococcus jannashii
15	6,503,703	Identification and use of antiviral compounds that inhibit interaction of host cell proteins and viral proteins required for viral replication
16	6,503,184	Human tumor necrosis factor receptor-like proteins TR11, TR11SV1 and TR11SV2
17	6,501,008	Maize endo-1,3;1,4-.beta.-glucanase nucleic acid
18	6,501,006	Nucleic acids conferring chilling tolerance
19	6,500,667	Aspartyl protease 2 (Asp2) antisense oligonucleotides
20	6,500,663	Unique associated Kaposi's sarcoma virus sequences and uses thereof
21	6,500,661	Enzymatic conversion of GDP-mannose to GDP-fucose
22	6,500,643	Human high affinity choline transporter
23	6,500,639	DNA shuffling to produce nucleic acids for mycotoxin detoxification
24	6,500,626	Cell death regulators
25	6,500,617	Optimization of pest resistance genes using DNA shuffling
26	6,500,613	Pneumococcal surface proteins and uses thereof
27	6,500,431	Inhibitors of angiogenesis and tumor growth
28	6,500,211	Mutant EGIII cellulase, DNA encoding such EGIII compositions and methods for obtaining same
29	6,495,667	Il-b30 antibodies
30	6,495,664	Fluorescent protein sensors of post-translational modifications
31	6,495,520	Apoptosis Inducing Molecule II and methods of use

APPENDIX A

List of first 500 of 892 U.S. Patents issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

32	6,495,348	Mitomycin biosynthetic gene cluster
33	6,495,322	RAIDD, a novel death adaptor molecule
34	6,495,129	Methods of inhibiting hematopoietic stem cells using human myeloid progenitor inhibitory factor-1 (MPIF-1) (Ckbeta-8/MIP-3)
35	6,495,128	Human chemokine .beta.-7 deletion and substitution proteins
36	6,492,577	Leafy cotyledon2 genes and their uses
37	6,492,158	Human kinesin protein HsKif6
38	6,492,151	Motor proteins and methods for their use
39	6,489,453	Chandra: a TH1-specific gene
40	6,489,146	End-complementary polymerase reaction
41	6,489,145	Method of DNA shuffling
42	6,489,138	Human ependymin
43	6,488,925	Macrophage inflammatory protein-4 (MIP-4) polypeptides
44	6,486,302	Hm2 cDNA and related polypeptide
45	6,486,301	Interleukin-20
46	6,485,925	Anthrax lethal factor is a MAPK kinase protease
47	6,485,719	Methods for inhibiting angiogenesis with leukocyte adhesion inhibitor-1 (LAI-1) polypeptides
48	6,484,105	Method for obtaining a plant with a genetic lesion in a gene sequence
49	6,483,011	Modified ADP-glucose pyrophosphorylase for improvement and optimization of plant phenotypes
50	6,482,923	Interleukin 17-like receptor protein
51	6,482,799	Self-preserving multipurpose ophthalmic solutions incorporating a polypeptide antimicrobial
52	6,482,647	Evolving susceptibility of cellular receptors to viral infection by recursive recombination
53	6,482,621	Compositions and methods for fumonisin detoxification
54	6,482,600	Breast cancer associated nucleic acid sequences and their associated proteins
55	6,479,731	Pi-ta gene conferring fungal disease resistance to plants
56	6,479,730	DNA Ligase II orthologue uses thereof
57	6,479,652	Oligonucleotide mediated nucleic acid recombination
58	6,479,642	Cortistatin: neuropeptides
59	6,479,634	IL-B30 proteins
60	6,479,629	Maize histone deacetylases and their use
61	6,479,258	Non-stochastic generation of genetic vaccines
62	6,479,254	Apoptosis inducing molecule II
63	6,476,297	Meiosis promoter
64	6,476,296	Nucleic acids that control seed and fruit development in plants
65	6,475,793	Genomic sequence of Rhizobium sp. NGR 234 symbiotic plasmid

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66	6,475,789	Human telomerase catalytic subunit: diagnostic and therapeutic methods
67	6,475,784	Inhibition of angiogenesis by delivery of nucleic acids encoding anti-angiogenic polypeptides
68	6,475,762	Phytase enzymes nucleic acids encoding phytase enzymes and vectors and host cells incorporating same
69	6,475,734	Polyhydroxyalkanoate synthase genes
70	6,475,492	Peptides and assays for the diagnosis of lyme disease
71	6,472,512	Keratinocyte derived interferon
72	6,472,197	GRB2 associating polypeptides and nucleic acids encoding therefor
73	6,472,140	alpha.-2- macroglobulin therapies and drug screening methods for Alzheimer's disease.
74	6,470,277	Techniques for facilitating identification of candidate genes
75	6,469,230	Starch debranching enzymes
76	6,468,984	DNA vaccine for protecting an avian against infectious bursal disease virus
77	6,468,978	Active hedgehog protein conjugate
78	6,468,768	Galectin 9 and 10SV polynucleotides
79	6,465,716	Nod factor binding protein from legume roots
80	6,465,633	Compositions and methods of their use in the treatment, prevention and diagnosis of tuberculosis
81	6,465,238	Gene encoding phosphoglucoisomerase
82	6,465,212	Leukotriene receptor
83	6,465,203	Glucan-containing compositions and paper
84	6,465,181	Reagents and methods useful for detecting diseases of the prostate
85	6,462,258	Plant expression constructs
86	6,462,254	Dual-tagged proteins and their uses
87	6,461,863	Modifying insect cell gylcosylation pathways with baculovirus expression vectors
88	6,461,855	Motor proteins and methods for their use
89	6,461,836	Molecular cloning of a 7TM receptor (AxOR34) and screening methods thereof
90	6,461,823	Death domain containing receptor-4 antibodies
91	6,458,930	Aspergillus fumigatus cofilin
92	6,458,532	Polynucleotides encoding IMP.18p myo-inositol monophosphatase and methods of detecting said polynucleotides
93	6,458,530	Selecting tag nucleic acids
94	6,455,668	Methods of diagnosing colorectal cancer, compositions, and methods of screening for colorectal cancer modulators
95	6,455,297	Methods and compositions for regulating cell death and enhancing disease resistance to plant pathogens

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96	6,455,293	Human kinesin-like protein HSKIF21B
97	6,455,254	Sequence based screening
98	6,455,040	Tumor necrosis factor receptor
99	6,452,069	SF3 promoter and methods of use
100	6,451,759	Noncleavable Fas ligand
101	6,451,562	Polypeptides encoding myeloid progenitor inhibitory factor-1 (MPIF-1) polynucleotides
102	6,451,539	Expression vectors, transfection systems, and method of use thereof
103	6,448,234	Compounds and methods for treatment and diagnosis of chlamydial infection
104	6,448,035	Family of immunoregulators designated leukocyte immunoglobulin-like receptor (LIR)
105	6,448,026	Screening assays for modulators of human kinesin protein HsKrp5
106	6,448,025	Motor proteins and methods for their use
107	6,448,020	Molecules associated with the human suppressor of fused gene
108	6,444,874	Hydroperoxide lyase gene from maize and methods of use
109	6,444,791	Methods and compositions for the treatment of keratoconus using protease inhibitors
110	6,444,790	Peptidoglycan recognition proteins
111	6,444,468	Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
112	6,444,440	Vanilloid receptor-2
113	6,441,151	Plant prohibition genes and their use
114	6,441,134	Isolated Candida albicans oligopeptide transporter gene
115	6,440,934	Angiogenically effective unit dose of FGF-2 and method of use
116	6,440,731	Polynucleotides encoding HsKrp5 a kinesin related protein
117	6,440,726	Expression vectors comprising multiple shear stress responsive elements (SSRE) and methods of use for treating disorders related to vasculogenesis and/or angiogenesis in a shear stress environment
118	6,440,698	Alzheimer's disease secretase, APP substrates therefor, and uses therefor
119	6,440,694	TNF-related death ligand
120	6,440,686	Methods for screening and therapeutic applications of kinesin modulators
121	6,440,685	Screening assays for modulators of human kinesin protein HsKif16b
122	6,440,684	Methods of identifying modulators of kinesin motor proteins
123	6,440,677	Nucleic acid affinity columns

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124	6,440,668	Method of DNA shuffling with polynucleotides produced by blocking or interrupting a synthesis or amplification process
125	6,437,115	Nucleic acids encoding KSP, a kinesin motor protein
126	6,436,686	Motor proteins and methods for their use
127	6,436,675	Use of codon-varied oligonucleotide synthesis for synthetic shuffling
128	6,433,249	Use of .beta.-glucosidase to enhance disease resistance and resistance to insects in crop plants
129	6,433,147	Death domain containing receptor-4
130	6,433,145	Keratinocyte derived interferon
131	6,432,916	Compounds and methods for treatment and diagnosis of chlamydial infection
132	6,432,707	Compositions and methods for the therapy and diagnosis of breast cancer
133	6,432,678	Macaca cynomolgus IL 18
134	6,432,671	Tryparedoxin, expression plasmid, process of production, method of use, test kit, and pharmaceutical composition
135	6,432,666	Dendritic cell receptor
136	6,432,660	Motor proteins and methods for their use
137	6,432,659	Motor proteins and methods for their use
138	6,432,645	Beta subunits of Slo family potassium channels
139	6,432,628	Caspase-14, an apoptotic protease, nucleic acids encoding and methods of use
140	6,429,362	Maize PR-1 gene promoters
141	6,429,304	Nucleic acids encoding a katanin p60 subunit
142	6,429,293	Sculpin-type antifreeze polypeptides and nucleic acids
143	6,429,005	Motor proteins and methods for their use
144	6,428,980	Nucleic acids encoding RIP3 associated cell cycle proteins
145	6,428,788	Compositions and methods for specifically targeting tumors
146	6,426,224	Oligonucleotide mediated nucleic acid recombination
147	6,426,207	Motor proteins and methods for their use
148	6,426,197	Polynucleotides encoding a human potassium channel
149	6,426,193	Screening assays for modulators of human kinesin protein HsKif21b
150	6,426,075	Protease-activatable pseudomonas exotoxin A-like proproteins
151	6,426,072	Compositions and methods for the therapy and diagnosis of lung cancer
152	6,423,544	Compositions and methods for producing recombinant virions
153	6,423,542	Oligonucleotide mediated nucleic acid recombination
154	6,423,513	Polynucleotides encoding protease-activatable pseudomonas exotoxin a-like proproteins

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155 6,421,613 Data processing of the maize prolifera genetic sequence
156 6,420,544 Polynucleotide and polypeptide sequences encoding murine organic anion transporter 5 (mOATP5)
157 6,420,534 Alzheimer's disease secretase, APP substrates therefor, and uses thereof
158 6,420,175 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
159 6,420,162 Nucleic acids encoding hskif16a, a kinesin motor protein
160 6,420,137 Nucleic acid encoding human neurotensin subtype 2 receptor
161 6,420,118 Peptides and peptidomimetics with structural similarity to human p53 that activate p53 function
162 6,420,116 Antimicrobial peptide
163 6,416,973 Nucleic acids encoding mammalian cell membrane protein MDL-1
164 6,416,966 Screening assays for modulators of human kinesin protein HsKif6
165 6,414,221 Transiently activated stress-inducible plant promoters
166 6,414,121 Human kinesin protein KSP
167 6,413,774 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
168 6,413,751 DNA adenine methyltransferases and uses thereof
169 6,413,745 Recombination of insertion modified nucleic acids
170 6,413,741 Human elk a voltage-gated potassium channel subunit
171 6,410,828 Regulatory sequences useful for gene expression in plant embryo tissue
172 6,410,687 Polypeptides for the detection of microtubule depolymerization inhibitors
173 6,410,245 Compositions and methods for detecting ligand-dependent nuclear receptor and coactivator interactions
174 6,410,233 Isolation and identification of control sequences and genes modulated by transcription factors
175 6,410,023 Recombinant parainfluenza virus vaccines attenuated by deletion or ablation of a non-essential gene
176 6,409,648 Polynucleotides encoding TRF1 binding proteins
177 6,407,315 Seed-preferred promoter from barley
178 6,407,211 Chimeric natriuretic peptides
179 6,407,046 Mutant EGIII cellulase, DNA encoding such EGIII compositions and methods for obtaining same
180 6,406,910 Recombination of insertion modified nucleic acids
181 6,406,907 Bovine tumor necrosis factor receptor-1 and methods of use
182 6,406,867 Antibody to human endokine alpha and methods of use
183 6,403,862 Seed-preferred promoter from maize
184 6,403,860 Ku80 homologue and uses thereof

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185 6,403,770 Antibodies to neutrokine-alpha
186 6,403,768 Manipulation of Mlo genes to enhance disease resistance in plants
187 6,403,557 Fibroblast growth factor-13
188 6,403,372 Aspergillus fumigatus profilin
189 6,403,351 Pyruvate carboxylase polypeptide from Corynebacterium glutamicum
190 6,399,573 Interleukin-1 receptor antagonist beta (IL-1rabeta)
191 6,399,346 Human kinesin-like protein HsKif16b
192 6,399,294 Nucleotide sequences of HIV-1 type (or subtype) O retrovirus antigens
193 6,395,962 Enhancing expression of a silenced target sequence in plants using plant viral enhancers and amplicons
194 6,395,547 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
195 6,395,540 Nucleic acids encoding HsKifC2, a kinesin motor protein
196 6,395,527 Motor proteins and methods for their use
197 6,395,514 Polynucleotides encoding chemokine.alpha.-5
198 6,395,306 Bee venom protein and gene encoding same
199 6,392,126 Adenosine deaminase homologues and uses thereof
200 6,392,026 Binding domains from plasmodium vivax and plasmodium falciparum erythrocyte binding proteins
201 6,392,024 Tenebrio antifreeze proteins
202 6,392,015 Method of identifying modulators of HIV-1 Vpu and Gag interaction with U binding protein (Ubp)
203 6,391,613 Motor proteins and methods for their use
204 6,391,601 Motor proteins and methods for their use
205 6,391,584 Expression-cloning method for identifying target proteins for eukaryotic tyrosine kinases and novel target proteins
206 6,391,573 Screening assays for modulators of human kinesin protein HSKIP3B
207 6,391,564 Methods and compositions utilizing Rad51
208 6,391,552 Enhancing transfection efficiency of vectors by recursive recombination
209 6,391,316 Vaccine compositions comprising Haemophilus somnus transferrin-binding proteins and methods of use
210 6,388,171 Compositions and methods for fumonisin detoxification
211 6,388,169 Maize orthologues of bacterial RecA proteins
212 6,388,066 MAR/SAR elements flanking RSYN7-driven construct
213 6,388,062 Modified p53 tetramerization domains having hydrophobic amino acid substitutions
214 6,388,052 NF-AT polypeptides and polynucleotides
215 6,387,702 Enhancing cell competence by recursive sequence recombination
216 6,387,679 Motor proteins and method for their use

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217	6,387,658	PCNA-associated cell cycle proteins, compositions and methods of use
218	6,387,644	Motor proteins and methods for their use
219	6,387,641	Crystallized P38 complexes
220	6,384,302	Trypsin inhibitors with insecticidal properties obtained from Pentaclethra macroloba
221	6,384,203	Family of immunoregulators designated leukocyte immunoglobulin-like receptors (LIR)
222	6,383,796	Nucleic acids encoding HSKIF21B, a kinesin motor protein
223	6,383,778	Nucleic acids encoding a G-protein coupled receptor involved in sensory transduction
224	6,380,183	Treatment of diseases involving cyst formation
225	6,379,964	Evolution of whole cells and organisms by recursive sequence recombination
226	6,379,941	Human kinesin-related protein HsKrp5
227	6,379,926	Polynucleotides encoding chemokine .beta.-6 antagonists
228	6,379,925	Angiogenic modulation by notch signal transduction
229	6,379,923	ELL2, a new member of an ELL family of RNA polymerase II elongation factors
230	6,379,912	Motor proteins and method for their use
231	6,379,671	Reagents and methods useful for detecting diseases of the breast
232	6,376,751	Nucleic acids encoding EMF1 that control reproductive development in plants
233	6,376,475	Control of immune responses by modulating activity of glycosyltransferases
234	6,376,246	Oligonucleotide mediated nucleic acid recombination
235	6,376,196	Recombinant neospora antigens and their uses
236	6,375,954	Size-variable strain-specific protective antigen for potomac horse fever
237	6,372,898	Human JAK3 variants
238	6,372,711	Methods for assaying human FSH using human FSH receptor
239	6,372,497	Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
240	6,372,473	Tissue plasminogen activator-like protease
241	6,372,456	Polynucleotides encoding chemokine .alpha.-6
242	6,372,454	Nucleic acid molecules encoding Follistatin-3
243	6,372,215	Monoclonal antibodies to human CD6
244	6,369,296	Recombinant plant viral vectors
245	6,369,201	Myostatin multimers
246	6,368,861	Oligonucleotide mediated nucleic acid recombination
247	6,368,841	Human kinesin-related protein HsKip3b
248	6,368,826	IGF-1 receptor interacting proteins
249	6,368,823	Kv potassium channel polypeptides and polynucleotides

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250 6,365,712 Methods and compositions for inhibiting inflammation and angiogenesis comprising a mammalian CD97 .alpha. subunit
251 6,365,408 Methods of evolving a polynucleotides by mutagenesis and recombination
252 6,365,377 Recombination of insertion modified nucleic acids
253 6,361,993 Human HSET motor proteins and methods for their use
254 6,361,975 Mouse aspartic secretase-2(mASP-2)
255 6,361,974 Exonuclease-mediated nucleic acid reassembly in directed evolution
256 6,358,742 Evolving conjugative transfer of DNA by recursive recombination
257 6,358,740 Recombination of insertion modified nucleic acids
258 6,358,725 Mouse aspartic secretase-1 (mASP1)
259 6,358,709 End selection in directed evolution
260 6,358,508 Antibodies to human tumor necrosis factor receptor TR9
261 6,355,471 Nucleic acids encoding Hskif16b, a kinesin motor protein
262 6,355,466 Motor proteins and methods for their use
263 6,355,465 Compounds
264 6,355,452 Human histamine H3 gene variant-2
265 6,355,447 Motor proteins and methods for their use
266 6,355,411 Virulence-associated nucleic acid sequences and uses thereof
267 6,352,859 Evolution of whole cells and organisms by recursive sequence recombination
268 6,352,842 Exonucease-mediated gene assembly in directed evolution
269 6,352,830 NF-AT polypeptides and polynucleotides and screening methods for immunosuppressive agents
270 6,352,694 Methods for inducing a population of T cells to proliferate using agents which recognize TCR/CD3 and ligands which stimulate an accessory molecule on the surface of the T cells
271 6,350,933 RG polynucleotides for conferring powdery mildew resistance in plants
272 6,350,597 Riboflavin synthase genes and enzymes and methods of use
273 6,348,586 Unique associated Kaposi's sarcoma virus sequences and uses thereof
274 6,348,573 Compositions and methods for identifying apoptosis signaling pathway inhibitors and activators
275 6,348,569 Spruce budworm antifreeze proteins, genes and method of using same
276 6,348,348 Human hairless gene and protein
277 6,346,655 Trichothecne-Resistant transgenic plants
278 6,346,410 Motor proteins and methods for their use

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279 6,346,379 Thermostable DNA polymerases incorporating nucleoside triphosphates labeled with fluorescein family dyes
280 6,344,549 ATR-2 cell cycle checkpoint
281 6,344,356 Methods for recombining nucleic acids
282 6,344,316 Nucleic acid analysis techniques
283 RE37,543 DNA sequence useful for the production of polyhydroxyalkanoates
284 6,342,656 Regulation of source-sink relationships and responses to stress conditions in plants
285 6,342,495 Agonists and antagonists of peripheral-type benzodiazepine receptors
286 6,342,382 Glycosyltransferases for biosynthesis of oligosaccharides, and genes encoding them
287 6,342,379 Detection of transmembrane potentials by optical methods
288 6,342,363 Death domain containing receptor 4 nucleic acids and methods
289 6,340,743 Antibodies to PIGR stalk
290 6,339,144 Proteins having insecticidal activities and method of use
291 6,335,198 Evolution of whole cells and organisms by recursive sequence recombination
292 6,335,189 Motor proteins and methods for their use
293 6,335,016 Chicken embryo lethal orphan (CELO) virus
294 6,333,184 Motor proteins and methods for their use
295 6,333,172 Genes and proteins controlling cholesterol synthesis
296 6,333,168 Cloning, expression and uses of dorsalin-1
297 6,333,155 Exploiting genomics in the search for new drugs
298 6,331,430 Motor proteins and methods for their use
299 6,331,424 Motor proteins and methods for their use
300 6,331,412 Methods and compounds for modulating male fertility
301 6,329,568 Tospovirus resistance in plants
302 6,329,567 Methods for improving seeds
303 6,329,504 Antifungal polypeptide and methods for controlling plant pathogenic fungi
304 6,326,472 Human receptor proteins; related reagents and methods
305 6,326,466 Double-stranded RNA dependent protein kinase derived peptides to promote proliferation of cells and tissues in a controlled manner
306 6,326,204 Evolution of whole cells and organisms by recursive sequence recombination
307 6,323,030 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
308 6,323,019 Design of novel highly efficient HIV based packaging systems for gene therapy
309 6,320,102 Leafy cotyledon1 genes and their uses
310 6,319,714 Oligonucleotide mediated nucleic acid recombination

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311 6,316,609 Nucleotide sequence of Escherichia coli pathogenicity islands
312 6,316,407 Antifungal polypeptide from alfalfa and methods for controlling plant pathogenic fungi
313 6,316,272 Methods of diagnosis of colorectal cancer and methods of screening for colorectal cancer modulators
314 6,316,253 Expression vectors, transfection systems, and method of use thereof
315 6,316,239 HKABY60 kinase family polypeptides
316 6,316,225 Human Prt1-like subunit protein (hPrt1) polynucleotides
317 6,316,195 Method for differentiating between the casual agents of karnal bunt wheat fungus and ryegrass smut using PCR
318 6,313,376 Maize aquaporins and uses thereof
319 6,313,375 Maize aquaporins and uses thereof
320 6,313,374 Method of using pelarogonium sp. as hyperaccumulators for remediating contaminated soil
321 6,312,941 Compositions and methods for identifying signaling pathway agonists and antagonists
322 6,312,937 Metalloproteinases
323 6,312,907 DbpA compositions and methods of use
324 6,312,899 NF-AT polypeptides and polynucleotides
325 6,310,273 Inhibiting apoptosis in plants using a baculovirus p35 protease inhibitor gene
326 6,309,858 T-type calcium channel variants; compositions thereof; and uses
327 6,309,822 Method for comparing copy number of nucleic acid sequences
328 6,309,634 Methods of treating Parkinson's disease using recombinant adeno-associated vector (rAAV)
329 6,307,020 Intracellular antifreeze polypeptides and nucleic acids
330 6,303,768 Methuselah gene, compositions and methods of use
331 6,303,749 Agouti and agouti-related peptide analogs
332 6,303,370 Tissue-specific regulatory elements
333 6,303,338 Pancreas-derived plasminogen activator inhibitor
334 6,303,301 Expression monitoring for gene function identification
335 6,303,295 Selenoproteins, coding sequences and methods
336 6,302,685 Human lysosomal protein and methods of its use
337 6,300,485 Myosin IXa and cyclic nucleotide gated channel-15 (CNGC-15) polynucleotides, polypeptides, compositions, methods, and uses thereof
338 6,300,477 Antibodies to human cystatin E
339 6,300,110 Peptides related to TPC2 and TPC3, two proteins that are coexpressed with telomerase activity
340 6,300,098 Human signal transduction serine/threonine kinase

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341 6,297,053 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
342 6,297,021 Ligand screening and design by X-ray crystallography
343 6,296,848 GRB2 associating polypeptides and nucleic acids encoding therefor
344 6,294,650 Inhibition of mammalian telomerase by peptide nucleic acids
345 6,294,379 Efficient AAV vectors
346 6,294,371 Motor proteins and methods for their use
347 6,294,343 Methods of diagnosing colorectal cancer, compositions, and methods of screening for colorectal cancer modulators
348 6,291,744 Nucleic acids encoding plant group 2 proteins and uses thereof
349 6,291,642 Mammalian cell cycle protein
350 6,291,242 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
351 6,291,223 Mouse aspartic secretase-1 (mASP1)
352 6,291,220 Polynucleotides encoding phosphatidylinositol 3-kinases
353 6,291,205 Method of increasing production of disulfide bonded recombinant proteins by saccharomyces cerevisiae
354 6,288,303 Rice .beta.-glucanase enzymes and genes
355 6,287,862 Evolution of whole cells and organisms by recursive sequence recombination
356 6,287,861 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
357 6,287,843 Maize histone deacetylases and their use
358 6,287,839 Cellulase producing actinomycetes, cellulase produced therefrom and method of producing same
359 6,287,575 Vaccine against papillomatous digital dermatitis (PDD)
360 6,284,949 Insect-resistant plants comprising a Bacillus thuringiensis gene
361 6,284,948 Genes and methods for control of nematodes in plants
362 6,284,486 Human oncogene induced secreted protein I
363 6,284,479 Substitutes for modified starch and latexes in paper manufacture
364 6,284,461 Use of inhibitors in reporter assays
365 6,284,456 Transcriptional coactivator that interacts with Tat protein and regulates its binding to TAR RNA, methods for modulating Tat transactivation, and uses therefor
366 6,280,950 Nucleic acid affinity columns
367 6,277,962 Receptor on the surface of activated t-cells: act-4
368 6,277,959 Isolated mammalian membrane protein genes; related reagents
369 6,277,638 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

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370 6,274,380 Cacnglike3 polynucleotides and expression systems
371 6,274,353 Method and compositions for improved polynucleotide synthesis
372 6,271,439 Methods and compositions for regulating cell death and enhancing disease resistance to plant pathogens
373 6,271,437 Soybean gene promoters
374 6,271,014 Mammalian proteinases; related reagents and methods
375 6,270,956 Transcriptional coactivator that interacts with Tat protein and regulates its binding to TAR RNA, methods for modulating Tat transactivation, and uses therefor
376 6,268,198 Cellulases and coding sequences
377 6,268,189 Fungal lactate dehydrogenase gene and constructs for the expression thereof
378 6,267,956 Protein activator and apoptosis
379 6,265,637 Genetic control of flowering
380 6,265,636 Pyruvate dehydrogenase kinase polynucleotides, polypeptides and uses thereof
381 6,265,177 Enzyme assay for mutant firefly luciferase
382 6,265,158 Ataxia-telangiectasia gene and its genomic organization
383 6,262,334 Human genes and expression products: II
384 6,262,333 Human genes and gene expression products
385 6,262,233 Tissue factor pathway inhibitor-3
386 6,262,018 Hypersensitive response elicitor from Erwinia amylovora and its use
387 6,261,801 Nucleic acids encoding tumor necrosis factor receptor 5
388 6,261,769 Intergenic spacer target sequence for detecting and distinguishing Chlamydial species or strains
389 6,261,760 Regulation of the cell cycle by sterols
390 6,258,777 Human B-cell translocation genes-2 and 3
391 6,258,536 Expression monitoring of downstream genes in the BRCA1 pathway
392 6,255,055 c-myc coding region determinant-binding protein (CRD-BP) and its nucleic acid sequence
393 6,252,057 Protein targeting to glycogen
394 6,251,674 Evolution of whole cells and organisms by recursive sequence recombination
395 6,251,632 Canine factor VIII gene, protein and methods of use
396 6,248,876 Glyphosate-tolerant 5-enolpyruvylshikimate-3-phosphate synthases
397 6,248,582 Gene deleted recombinant FeLV proviral DNA for production of vaccines against FeLV
398 6,248,550 Assays for protein kinases using fluorescent protein substrates
399 6,248,543 Compositions and methods for screening antimicrobials
400 6,248,517 Decorin binding protein compositions and methods of use

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401 6,245,886 Peptides and peptidomimetics with structural similarity to human P53 that activate P53 function
402 6,242,668 Strawberry endo-1,4-.beta.-glucanase genes and their uses
403 6,242,566 Ligand (ACT-4-L) to a receptor on the surface of activated CD4+ T-cells
404 6,242,238 Isolated nucleic acid molecule encoding mammalian endoglucuronidase and uses therefor
405 6,238,888 Keratinocyte growth factor-2 formulations
406 6,238,884 End selection in directed evolution
407 6,235,975 Leafy cotyledon1 genes and methods of modulating embryo development in transgenic plants
408 6,235,972 Maize Rad23 genes and uses thereof
409 6,235,883 Human monoclonal antibodies to epidermal growth factor receptor
410 6,235,881 Polypeptides encoded by novel HIV-2 proviruses
411 6,235,510 ppGaNTase-T6
412 6,235,278 Biological insect control agents expressing insect-specific toxin genes, methods and compositions
413 6,232,527 Maize Rad2/FEN-1 orthologues and uses thereof
414 6,232,457 Recombinant vanadium haloperoxidases and their uses
415 6,232,110 Coding sequence for protein phosphatase methylesterase, recombinant DNA molecules and methods
416 6,232,100 Cortistatin Polypeptides
417 6,229,064 Nucleic acids that control endosperm development in plants
418 6,228,992 Proteins for control of nematodes in plants
419 6,228,623 Polyhydroxyalkanoates of narrow molecular weight distribution prepared in transgenic plants
420 6,228,591 Polycystic kidney disease PKD2 gene and uses thereof
421 6,225,532 Tomato CF-5 gene encoding a disease resistance polypeptide
422 6,225,456 Ras suppressor SUR-5
423 6,225,086 Polynucleotides encoding ankyrin proteins
424 6,222,095 Sequences from auxin-induced gene products targeting fusion proteins for degradation
425 6,222,019 Human IRAK-2 antibodies
426 6,221,597 Essential genes of yeast as targets for antifungal agents, herbicides, insecticides and anti-proliferative drugs
427 6,218,523 Prostate cancer-specific marker
428 6,215,048 Nucleic acid sequences encoding an antifungal polypeptide, aly AFP from alyssum and methods for their use
429 6,214,588 Factors which modify gene transcription and methods of use therefor
430 6,214,580 Human tumor necrosis factor receptor tr10

APPENDIX A

List of first 500 of 892 U.S. Patents issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

431	6,214,355	DbpA compositions
432	6,211,440	Hm2 cDNA from maize encoding disease resistance polypeptide
433	6,211,435	Amino polyol amine oxidase polynucleotides and related polypeptides and methods of use
434	6,211,434	Amino polyol amine oxidase polynucleotides and related polypeptides and methods of use
435	6,211,433	Manipulation of Mlo genes to enhance disease resistance in plants
436	6,211,430	FbLate promoter
437	6,211,336	Ataxia-telangiectasia gene
438	6,211,164	Antisense oligonucleotides of the human chk1 gene and uses thereof
439	6,210,933	Recombinant .alpha.-2,3-sialyltransferases and their uses
440	6,210,671	Humanized antibodies reactive with L-selectin
441	6,210,670	Cross-reacting monoclonal antibodies specific for E-selectin and P-selectin
442	6,207,432	Tyrosylprotein sulfotransferases and methods of use thereof
443	6,207,414	Tyrosylprotein sulfotransferases and methods of use thereof
444	6,207,380	Reagents and methods useful for detecting diseases of the urinary tract
445	6,204,437	DNA constructs and plants incorporating them
446	6,204,040	Gluconobacter suboxydans sorbitol dehydrogenase, genes and methods of use thereof
447	6,204,017	Polynucleotide encoding a histamine receptor
448	6,204,016	Tyrosylprotein sulfotransferases and methods of use thereof
449	6,200,811	Cell transformation vector comprising an HIV-2 packaging site nucleic acid and an HIV-1 GAG protein
450	6,200,803	Essential genes of yeast as targets for antifungal agents, herbicides, insecticides and anti-proliferative drugs
451	6,200,763	Myeloid cell leukemia associated gene mcl-1
452	6,200,749	Mutated forms of the ataxia-telangiectasia gene and method to screen for a partial A-T phenotype
453	6,198,020	Nitric oxide as an activator of the plant pathogen defense systems
454	6,197,925	NF-AT polypeptides and polynucleotides
455	6,197,517	Essential genes of yeast as targets for antifungal agents, herbicides, insecticides and anti-proliferative drugs
456	6,197,069	Adrenomedullin receptor polynucleotides
457	6,194,638	Alteration of hemicellulose concentration in plants
458	6,194,637	Maize DNA ligase I orthologue and uses thereof
459	6,194,547	ETS2 repressor factor (ERF)

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List of first 500 of 892 U.S. Patents issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

460 6,191,260 Brain-associated inhibitor of tissue-type plasminogen activator
461 6,190,189 Cellulases and coding sequences
462 6,187,909 Viral encoded semaphorin protein receptor polypeptides
463 6,187,560 Polynucleotides and polypeptides belonging to the uncoupling proteins family
464 6,187,559 Phospholipase D gene
465 6,184,355 FAE1 genes and their uses
466 6,184,202 Cell death regulators
467 6,184,018 .beta.-glucosidase coding sequences and protein from orpinomyces PC-2
468 6,183,990 Compounds
469 6,183,988 Leukocyte-specific protein and gene, and methods of use thereof
470 6,183,961 Methods and compositions for regulating cell cycle progression
471 6,183,751 Unique associated Kaposi's Sarcoma virus sequences and uses thereof
472 6,180,850 Maize Ku70 orthologue and uses thereof
473 6,180,774 Synthetic DNA sequences having enhanced expression in monocotyledonous plants and method for preparation thereof
474 6,180,406 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
475 6,180,112 Pasteurella haemolytica vaccine
476 6,177,611 Maize promoters
477 6,175,058 Nucleic acid sequence encoding FLP recombinase
478 6,174,689 Viral encoded semaphorin protein receptor DNA and polypeptides
479 6,174,676 Cytokine-stress- and oncoprotein-activated human protein kinase kinases
480 6,174,532 L2 immunogenic peptides of papillomavirus
481 6,174,528 Synthetic peptides and vaccines comprising same
482 6,172,211 Nucleic acid encoding tag7 polypeptide
483 6,171,833 Pyruvate carboxylase from corynebacterium glutamicum
484 6,171,820 Saturation mutagenesis in directed evolution
485 6,171,816 Human XAG-1 polynucleotides and polypeptides
486 6,171,781 NF-AT polypeptides and polynucleotides
487 6,171,590 Chemokine receptor peptide for inducing an immune response
488 6,169,073 Peptides and peptidomimetics with structural similarity to human p53 that activate p53 function
489 6,166,301 Method for assaying genetic attributes in cotton fiber cells
490 6,166,195 Nematode-active toxins and genes which code therefor
491 6,166,182 Human neurotensin receptor type 2 and splice variants thereof

APPENDIX A

List of first 500 of 892 U.S. Patents issued from 1976 to present containing terms "BESTFIT" and "protein" in all fields

492 6,166,178 Telomerase catalytic subunit
493 6,165,793 Methods for generating polynucleotides having desired characteristics by iterative selection and recombination
494 6,162,632 OxlT sequence and its use
495 6,159,469 Withdrawn
496 6,156,878 Ligand (ACT-4-L) to a receptor on the surface of activated CD4.sup.+ T-cells
497 6,156,310 Topoisomerase III
498 6,153,430 Nucleic acid encoding mesothelin, a differentiation antigen present on mesothelium, mesotheliomas and ovarian cancers
499 6,153,402 Death domain containing receptors
500 6,150,132 Chemokine receptor able to bind to MCP-1, MIP-1.alpha. and/or RANTES. Its uses

APPENDIX B
Description of BESTFIT Program

APPENDIX B
Description of BESTFIT Program

BestFit makes an optimal alignment of the best segment of similarity between two sequences. Optimal alignments are found by inserting gaps to maximize the number of matches using the local homology algorithm of Smith and Waterman.

BestFit inserts gaps to obtain the optimal alignment of the best region of similarity between two sequences, and then displays the alignment in a format similar to the output from Gap. The sequences can be of very different lengths and have only a small segment of similarity between them. You could take a short RNA sequence, for example, and run it against a whole mitochondrial genome.

BestFit is the most powerful method in the Wisconsin Package(TM) for identifying the best region of similarity between two sequences whose relationship is unknown.

BestFit uses the local homology algorithm of Smith and Waterman (Advances in Applied Mathematics 2; 482-489 (1981)) to find the best segment of similarity between two sequences. BestFit reads a scoring matrix that contains values for every possible GCG symbol match (see the LOCAL DATA FILES topic below) . The program uses these values to construct a path matrix that represents the entire surface of comparison with a score at every position for the best possible alignment to that point. The quality score for the best alignment to any point is equal to the sum of the scoring matrix values of the matches in that alignment, less the gap creation penalty times the number of gaps in that alignment, less the gap extension penalty times the total length of all gaps in that alignment. The gap creation and gap extension penalties are set by you. If the best path to any point has a negative value, a zero is put in that position.
After the path matrix is complete, the highest value on the surface of comparison represents the end of the best region of similarity between the sequences. The best path from this highest value backwards to the point where the values revert to zero is the alignment shown by BestFit. This alignment is the best segment of similarity between the two sequences. See, http://www.biology.wustl.edu/gcg/bestfit.html#function.

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

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(excerpts from specification shown in italics)

U.S. Patent No. 5,871,969
Hastings , et al. February 16, 1999

United States Patent 5,968,780
Fan , et al. October 19, 1999

United States Patent 5,985,614
Rosen , et al November 16, 1999

United States Patent 5,998,171
Yu , et al. December 7, 1999

United States Patent 6,011,012
Ni , et al. January 4, 2000

United States Patent 6,027,916
Ni , et al. February 22, 2000

United States Patent 6,028,169
Kreider , et al. February 22, 2000

United States Patent 6,096,515
Crabtree , et al. August 1, 2000

United States Patent 6,130,079
Ni , et al. October 10, 2000

United States Patent 6,143,498
Olsen , et al. November 7, 2000

United States Patent 6,150,099
Crabtree , et al. November 21, 2000

United States Patent 6,171,781
Crabtree , et al. January 9, 2001

United States Patent 6,171,816
Yu , et al. January 9, 2001

United States Patent 6,174,532

APPENDIX C
Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

Campo , et al. January 16, 2001

United States Patent 6,242,566
Godfrey ,et al. June 5, 2001

United States Patent 6,261,801
Wei , et al. July 17, 2001

United States Patent 6,284,486
Olsen , et al. September 4, 2001

United States Patent 6,329,568
Gonsalves , et al. December 11, 2001

United States Patent 6,388,052
Crabtree , et al. May 14, 2002

United States Patent 6,403,557
Greene , et al. June 11, 2002

United States Patent No. 6,562,593
Merkulov , et al. May 13, 2003

United States Patent No. 6,541,233
Hillen , et al. April 1, 2003

United States Patent No. 6,497,880
Wisniewski December 24, 2002

United States Patent 6,391,847
Evans , et al. May 21, 2002

United States Patent No. 6,093,535
Mori , et al. July 25, 2000

United States Patent No. 5,830,740
Miller , et al. November 3, 1998

United States Patent No. 5,695,960
Chan , et al. December 9, 1997

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(excerpts from specification shown in italics)

United States Patent No. 6,562,593
Merkulov , et al. May 13, 2003

Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof

Appl. No.: **740041** Filed: **December 20, 2000**
The present application claims priority to provisional applications U.S. Ser. No. 60/251,035 filed Dec. 5, 2000.

Claim 17. An isolated nucleic acid molecule encoding a human transporter peptide, said nucleic acid molecule sharing at least 90 ***percent homology*** with a nucleic acid molecule shown in SEQ ID NO:1.

To determine the percent identity of two amino acid sequences or two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, at least 30%, 40%, 50%, 60%, 70%, 80%, or 90% or more of a reference sequence is aligned for comparison purposes. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in

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(excerpts from specification shown in italics)

Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., et al., Nucleic Acids Res. 12(1):387 (1984)) (available at http://www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Myers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (J. Mol. Biol. 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (Nucleic Acids Res. 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used.

Full-length pre-processed forms, as well as mature processed forms, of proteins that comprise one of the peptides of the present invention can readily be identified as having complete sequence identity to one of the transporter peptides of the present invention as well as being encoded by the same genetic locus as the transporter peptide provided herein.

Allelic variants of a transporter peptide can readily be identified as being a human

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

protein having a high degree (significant) of sequence homology/identity to at least a portion of the transporter peptide as well as being encoded by the same genetic locus as the transporter peptide provided herein. Genetic locus can readily be determined based on the genomic information provided in FIG. 3, such as the genomic sequence mapped to the reference human. As indicated by the data presented in FIG. 3, the map position was determined to be on chromosome 12 by ePCR, and confirmed with radiation hybrid mapping. As used herein, two proteins (or a region of the proteins) have significant homology when the amino acid sequences are typically at least about 70-80%, 80-90%, and more typically at least about 90-95% or more homologous. A significantly homologous amino acid sequence, according to the present invention, will be encoded by a nucleic acid sequence that will hybridize to a transporter peptide encoding nucleic acid molecule under stringent conditions as more fully described below.

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

United States Patent No. 6,541,233
Hillen , et al. April 1, 2003

.beta.-glucanase from a bacillus

Appl. No.: **463862**
Filed: **May 1, 2000**
PCT Filed: **July 21, 1998**
PCT NO: **PCT/EP98/04564**
PCT PUB.NO.: **WO99/06573**
PCT PUB. Date: **February 11, 1999**
Foreign Application Priority Data
Jul 30, 1997[DE] 197 32 751

Claim 4. An isolated polynucleotide comprising the sequence SEQ ID NO:2 or a polynucleotide with more than 70 ***percent homology*** to SEQ ID NO:2, wherein said polynucleotide encodes a polypeptide with .beta.-glucanolytic activity.

Claim 5. The polynucleotide of claim 4 which is 75 to 99 percent homologous to the sequence reproduced in SEQ ID-NO:2.

Claim 7. An isolated polypeptide with .beta.-glucanolytic activity and a homology of more than 70 percent to the polypeptide with the amino acid sequence SEQ ID NO:1.

Claim 8. The polypeptide of claim 7 with a homology of 75 to 99 percent to the polypeptide with the amino acid sequence SEQ ID NO:1.

A .beta.-glucanase according to the invention preferably has a homology of more than 70%, more particularly 75% to 99%, to the .beta.-glucanase from Bacillus alkalophilus DSM 9956. The same applies to the basic gene.

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(excerpts from specification shown in italics)

United States Patent No. 6,497,880
Wisniewski December 24, 2002

Heat shock genes and proteins from Neisseria meningitidis, Candida glabrata and Aspergillus fumigatus

Appl. No.: **207388** Filed: **December 8, 1998**

Claim 2. An isolated polypeptide comprising an amino acid sequence that is at least 95% homologous to the protein encoded by SEQ ID NO:5, wherein the polypeptide comprises a peptide of at least 8 contiguous amino acids of the protein encoded by SEQ ID NO:5, wherein the peptide binds to a major histocompatibility complex molecule, and wherein ***percent homology*** is determined according to an algorithm incorporated in a protein database search program used in BLAST (BLAST.TM., a computer program) or DNA STAR MEGALIGN (DNA STAR MEGALIGN.TM., a computer program).

In certain embodiments, the isolated Hsp60 polypeptide is derived from proteolytic cleavage or chemical synthesis, or is an expression product of a transformed host cell containing a nucleic acid molecule encoding the Hsp60 or portion thereof. In further certain embodiments, the isolated Hsp60 polypeptide comprises greater than 95% homology to the Hsp60 polypeptide of FIG. 21, and the isolated Hsp60 polypeptide is able to be selectively bound by an antibody specific for a Candida glabrata Hsp60.

Within the context of this invention, it should be understood that Hsp70 and Hsp60 include wild-type/native protein sequences, as well as other variants (including alleles) and fragments of the native protein sequences. Briefly, such variants may result from natural polymorphisms or be synthesized by recombinant methodology or chemical synthesis, and differ from wild-type proteins by one or more amino acid substitutions, insertions, deletions, or the like. Further, in the region of homology to the native sequence, a variant should preferably have at least 95% amino acid sequence homology, and within certain embodiments, greater than 97% or 98% homology. As used herein, amino acid "homology" is determined by a computer algorithm incorporated in a protein database search program commonly used in the art, and more particularly, as incorporated in the programs BLAST (BLAST.TM., a computer program) (Altschul et al., Nucleic Acids Res. (25) 3389-3402, 1997) or DNA STAR MEGALIGN (DNA STAR MEGALIGN.TM., a computer program) which return similar results in

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(excerpts from specification shown in italics)

homology calculations. As will be appreciated by those of ordinary skill in the art, a nucleotide sequence encoding an Hsp or a variant may differ from the native sequences presented herein due to codon degeneracies, nucleotide polymorphisms, or nucleotide substitutions, deletions or insertions.

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(excerpts from specification shown in italics)

United States Patent 6,391,847
Evans , et al. May 21, 2002

Method, polypeptides, nucleotide sequence of XOR-6, a vitamin D-like receptor from xenopus

Appl. No.: **875082**
Filed: **July 17, 1997**
PCT Filed: **January 16, 1996**
PCT NO: **PCT/US96/00058**
371 Date: **July 17, 1997**
102(e) Date: **July 17, 1997**
PCT PUB.NO.: **WO96/22390**
PCT PUB. Date: **July 25, 1996**
This application is a filing under 35 U.S.C. .sctn.371 from PCT/US96/00058, filed Jan. 16, 1996; which is a continuation-in-part and claims priority to U.S. patent application Ser. No. 08/374,445; filed Jan. 17, 1995, now abandoned

Claim 14. A method of testing a compound for its ability to regulate transcription-activating effects of a nuclear receptor polypeptide wherein said receptor comprises a DNA binding domain having at least about 73 ***percent homology*** with residues 37-102 of the amino acid sequence of SEQ ID NO:2, said method comprising assaying for a change in expression of reporter protein upon contacting of test cells with said compound, as compared to the expression of said reporter protein in the absence of said compound, and identifying as a compound that regulates the transcription-activating effects of said receptor those which cause a change in expression of said reporter protein when compared to the expression of said reporter in the absence of said compound;
wherein said test cell comprises said receptor polypeptide and reporter vector,
wherein said reporter vector comprises:
(a) a promoter that is operable in said test cell,
(b) a hormone response element for said receptor, and
(c) DNA encoding said reporter protein,
wherein said reporter protein-encoding DNA is operatively linked to said promoter for transcription of said DNA,
wherein said promoter is operatively linked to said hormone response element for activation thereof by said receptor polypeptide.

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

Claim 16. A method according to claim 14, wherein said receptor further comprises: a ligand binding domain having at least about 42 percent homology to residues 183-386 of the amino acid sequence of SEQ ID NO:2.

As used herein, nucleotide sequences which are substantially the same share at least about 90% identity, and amino acid sequences which are substantially the same typically share more than 95% amino acid identity. It is recognized, however, that proteins (and DNA or mRNA encoding such proteins) containing less than the above-described level of homology arising as splice variants or that are modified by conservative amino acid substitutions (or substitution of degenerate codons) are contemplated to be within the scope of the present invention.

FIG. 1 presents a schematic comparison between XOR-6 and the human vitamin D3 receptor. The two amino acid sequences were aligned using the program GAP (see Devereaux et al., in Nucl. Acids Res. 12:387-395 (1984)). Similarity between XOR-6 and hVDR is expressed as percent amino acid identity.

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(excerpts from specification shown in italics)

United States Patent No. 6,093,535
Mori , et al. July 25, 2000

Method for identifying attenuated chickenpox virus Oka strain or strain originating therein and acceptable as attenuated chickenpox vaccine virus

Appl. No.: **983045**
Filed: **January 15, 1998**
PCT Filed: **May 15, 1997**
PCT NO: **PCT/JP97/01646**
371 Date: **January 15, 1998**
102(e) Date: **January 15, 1998**
PCT PUB.NO.: **WO97/43420**
PCT PUB. Date: **November 20, 1997**
Foreign Application Priority Data
May 15, 1996[JP] 8-158795
The application claims the benefit under 35 U.S.C. .sctn.371 of prior PCT International Application No. PCT/JP97/01646 which has an international filing date of May 15, 1997 which designated the United States of America, the entire contents of which are hereby incorporated by reference.

Claim 1. A method for identifying the attenuated varicella virus Oka strain or a strain derived therefrom which functions as an effective component of an attenuated variceila vaccine, which comprises:
analyzing a genomic DNA and DNA fragments thereof present in a sample of varicella virus;
determining whether the analyzed genomic DNA and DNA fragments thereof of said sample of varicella virus satisfy eight characteristics (A1) to (A8) defined below; and
identifying said sample of varicella virus as the attenuated varicella virus Oka strain or a strain derived therefrom which functions as an effective component of an attenuated varicella live vaccine when said sample satisfies all of the following eight characteristics (A1) to (A8):
(A1) the size of the K fragment obtained by digesting the varicella virus genomic DNA with the restriction enzyme HpaI is 3231 bp;
(A2) the size of the P fragment obtained by digesting the varicella virus genomic DNA with the restriction enzyme EcoRI is 1749 bp;

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(excerpts from specification shown in italics)

(A3) when a DNA fragment which is amplified from the varicella virus genomic DNA by PCR using the PCR primer 1 (SEQ ID NO. 3) and the PCR primer 3 (SEQ ID NO. 5) is treated with the restriction enzyme AccIII, the DNA fragment is cleaved into two parts having sizes of 1208 bp and 556 bp, respectively;
(A4) a DNA fragment which is amplified from the varicella virus genomic DNA by PCR using the PCR primer 2 (SEQ ID NO. 4) and the PCR primer 3 (SEQ ID NO. 5) has a size of 487 bp;
(A5) the varicella virus genomic DNA and the attentuated varicella virus Oka strain genomic DNA exhibit substantially the same electrophoretic mobility with respect to a DNA fragment determined by PCR-SSCP wherein the PCR primer 2 (SEQ ID NO. 4) and the PCR primer 3 (SEQ ID NO. 5) are used in the PCR of said PCR-SSCP;
(A6) a DNA fragment which is amplified from the varicella virus genomic DNA by PCR using the PCR primer PS1 (SEQ ID NO. 7) and the PCR primer PS2 (SEQ ID NO. 8) lacks a restriction enzyme PstI cleavage site;
(A7) the homology between the 162 amino acid sequence coded by the 487 bp DNA fragment amplified from the varicella virus genomic DNA by PCR using the PCR primer 2 (SEQ ID NO. 4) and the PCR primer 3 (SEQ ID NO. 5), and the 162 amino acid sequence of SEQ ID NO. 1 is 98 to 100%, wherein the ***percent homology*** is represented by the following formula (1):
{(162-n)/162.times.100 (1)
wherein n represents the number of different amino acids; and
(A8) the homology between the 560 amino acid sequence coded by the entire coding region of Gene14, and the 560 amino acid sequence of SEQ ID NO. 2 is 99 to 100%, wherein the ***percent homology*** is represented by the following formula (2):
{(560-n)/560}.times.100 (2)
wherein n represents the number of different amino acids.

Further, the nucleotide sequence of each of the R2-487 regions was determined by Cycle Sequence Kit (manufactured and sold by TAKARA SHUZO Co. Ltd., Japan; Manual Code No. R014). The nucleotide sequences of the R2-487 regions of the samples were individually compared with the nucleotide sequence of the attenuated Oka strain to determine the DNA homology between the nucleotide sequences, and also, the amino acid sequences of the R2-487 regions of the samples which were obtained by translating the nucleotide sequences in accordance with the universal code were individually compared with that of the Oka strain to determine the homology between the amino acid sequences. The determination was performed by a computer software for gene analysis {GENETYX (ver. 9.0)(A computer Software for analyzing

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(excerpts from specification shown in italics)

genes and proteins; manufactured and sold by Software Development Co., Ltd., Japan}. The nucleotide sequence and amino acid sequence of the R2-487 region of the attenuated Oka strain are shown in SEQ ID NO. 1.

The comparison between the nucleotide sequence of the R2-487 region of the attenuated Oka strain and the nucleotide sequence of each of the 10 samples including the Kawaguchi strain shows that a difference in nucleotides was found with respect to 4 or more nucleotides in the R2-487 region of each of the samples, and that this difference in the nucleotides was accompanied by a change in amino acids (coded by 162 codons, i.e., 162 codons=487 bp/3). Thus, the homology between the amino acid sequence of the attenuated Oka strain and that of each of the 10 samples was less than 98% {i.e., 487 bp/3=162 codons; [(162 codons-4 different codons)/162 codons].times.100=97.5% <98%}.

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(excerpts from specification shown in italics)

United States Patent No. 5,830,740
Miller , et al. November 3, 1998

Serine protease operative between 75.degree.C. and 103.degree.C.

Appl. No.: **278042** Filed: **July 20, 1994**

Claim 4. An isolated and purified serine protease which exhibits proteolytic activity at temperature of between about 75.degree. C. and about 130.degree. C., said protease comprising an amino acid sequence having at least 90 ***percent homology*** to SEQ ID NO:3.

Claim 5. An isolated and purified serine protease which exhibits proteolytic activity at temperature of between about 75.degree. C. and about 130.degree. C., said protease comprising an amino acid sequence having at least 90 ***percent homology*** to SEQ ID NO:2.

FIGS. 5A, 5B and 5C are pictorial representations of three-dimensional models of aerolysin. The models were built using the Biosyn Homology program with the tertiary structure of the thermitase as a starting point. Residue numbering follows equivalent sites in the P. aerophilum sequence. Numbering of secondary structure elements is from FIGS. 6 and 7. FIG. 5A shows clustering of thermophilic residues from two surface loops L1 and L3; FIG. 5B shows thermophilic sites in two adjacent extended strands E6 and E7 linked by loop L8; and FIG. 5C shows thermophilic sites on each side of surfaces helices III and IV.

The translated amino acid sequence (FIG. 1 and sequence ID No. 2) shows a long open reading frame starting 83 amino acids upstream of sequence homology to various subtilisins. The first 15 amino acids encoded by this region showed similarities to leader sequences from subtilisins Carlsberg, BPN', 1168 and T. aquaticus aqualysin I. The intervening region is not homologous to any known protein and appears to be the N-terminal peptide autocatalytically cleaved on subtilisin's export from the cell (Terada et al. 1990). The amino acid sequence of the proteolytically active enzyme remaining after cleavage is set forth in sequence ID No. 3. Based on these considerations, methionine was assigned as the initiator for the protein, as well as a potential cleavage site for the mature protein. The end of the gene is clearly defined by 5 stop codons. The first stop

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codon appeared 15 bases upstream, comparable in position to the end of the gene in several Bacillus species, and was followed by a poly T region.

The alignment similarity scores identified the P. aerophilum sequence as most similar to Gram-positive subtilisins, but PredictProtein identified thermitase from Thermoactinomyces vulgaris (16) as having the most similar structure. Similarity to other serine proteases was much weaker. In particular, the P. aerophilum sequence showed weak homology to aqualysin I. produced by Thermus aquaticus (17), and halolysin, a serine protease from a moderately thermophilic (60.degree. C.) and halophilic archaeum (18). Neutral proteases such as thermolysin (19), despite their structural similarity, were not recovered by BLAST or PredictProtein, and were not included in the alignment.

The above multiple sequence alignment of aerolysin with 14 different serine type proteases shows that subtilisins from Gram-positive bacteria, rather than archaeal or eukaryal serine proteases, have the greatest homology. In view of the above demonstrated relationship of aerolysin to subtilisins, aerolysin will be useful in the same type of applications in which these other subtilisins and serine proteases are presently being used.

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United States Patent No. 5,695,960
Chan , et al. December 9, 1997

Hippuricase gene

Appl. No.: **485216**
Filed: **June 7, 1995**
This application is continuation of PCT/CA94/00270, filed May 13, 1994, which is a continuation-in-part of U.S. Ser. No. 08/061,696, filed May 14, 1993, now abandoned.

Claim 5. A method for preparing hippuricase comprising:
(a) transferring a recombinant expression vector containing a nucleic acid molecule encoding a polypeptide having the amino acid sequence and enzymatic activity of Campylobacter jejuni hippuricase into a host cell; (b) selecting transformed host cells from untransformed host cells; (c) culturing a selected transformed host cell under conditions which allow expression of the polypeptide; and (d) isolating the polypeptide.

Claim 6. A method according to claim 5 wherein said polypeptide has the amino acid sequence as shown in the Sequence Listing as SEQ ID NO:1, or a sequence having between 97 and 100 ***percent homology*** thereto, having the enzymatic activity of Campylobacter jejuni hippuricase.

Claim 7. A method according to claim 5 wherein said nucleic acid comprises (a) a nucleic acid sequence as shown in SEQ ID:1 and FIG. 1, wherein T can also be U; (b) nucleic acid sequences complementary to (a); or (c) nucleic acid sequences which are at least 85% homologous to (a).

The invention still further provides a purified and isolated polypeptide having part or all of the primary structural confirmation (ie. continuous sequence of amino acid residues) and the enzymatic activity of hippuricase. In a preferred embodiment the polypeptide has an amino acid sequence as shown in FIG. 1 and in the Sequence Listing as SEQ ID NO:1 and NO:2, or a sequence having between 97 and 100 percent homology thereto.

It will be appreciated that the invention includes nucleotide or amino acid sequences which have substantial sequence homology with the nucleotide and amino acid sequences shown in the Sequence Listing as SEQ ID NO:1 and NO:2. The term "sequences having substantial sequence homology" means those nucleotide and amino

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acid sequences which have slight or inconsequential sequence variations from the sequences disclosed in the Sequence Listing as SEQ ID NO:1 and NO:2 i.e. the homologous sequences function in substantially the same manner to produce substantially the same polypeptides as the actual sequences. The variations may be attributable to local mutations or structural modifications. It is expected that a sequence having 85-90% sequence homology with the DNA sequence of the invention will provide a functional hippuricase polypeptide.

Nucleic acid sequences having substantial sequence homology include nucleic acid sequences having at least 85%, preferably at least 90% homology with the nucleic acid sequence as shown in SEQ. ID. NO:1 and in FIG. 1; and fragments thereof having at least 15 to 30, preferably at least 15 bases, most preferably 20 to 30, which will hybridize to these sequences under stringent hybridization conditions. Stringent hybridization conditions are those which are stringent enough to provide specificity, reduce the number of mismatches and yet are sufficiently flexible to allow formation of stable hybrids at an acceptable rate. Such conditions are known to those skilled in the art and are described, for example, in Sambrook, et al, (1989, Molecular Cloning, A Laboratory Manual, Cold Spring Harbor). By way of example only, stringent hybridization with short nucleotides may be carried out at 5.degree.-10.degree. below the T.sub.m using high concentrations of probe such as 0.01-1.0 pmole/ml.

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U.S. Patent No. 5,871,969
Hastings , et al. February 16, 1999

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a member selected from the group consisting of:
(a) a nucleotide sequence encoding a full-length Neuronal Attachment Factor-1 (NAF-1) polypeptide having the complete amino acid sequence in SEQ ID NO:2, or the complete amino acid sequence encoded by the cDNA clone contained in the ATCC Deposit No. 97343;
(b) a nucleotide sequence encoding amino acids 2 to 331 (SEQ ID NO:2) of a full-length NAF-1 polypeptide or the complete amino acid sequence excepting the N-terminal methionine encoded by the cDNA clone contained in the ATCC Deposit No. 97343;
(c) a nucleotide sequence encoding a predicted mature form of the NAF-1 polypeptide having the amino acid sequence at positions 24 to 331 in SEQ ID NO:2 or as encoded by the cDNA clone contained in the ATCC Deposit No. 97343;
(d) a nucleotide sequence encoding a predicted mature form of the NAF-1 polypeptide having the amino acid sequence at positions 27 to 331 in SEQ ID NO:2 or as encoded by the cDNA clone contained in the ATCC Deposit No. 97343; and
(e) a nucleotide sequence fully complementary to any of the nucleotide sequences in (a), (b), (c) or (d) above;
wherein percentage of identity is determined using the Bestfit program with parameters set such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and gaps of up to 5% of the total number of nucleotides in the reference sequence are allowed, and wherein up to 5% of the amino acid residues in the reference sequence may be deleted or substituted with another amino acid, or a number of amino acids up to 5% of the total amino acid residues in the reference sequence may be inserted into the reference sequence.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1 or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 5371 1). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-

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489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

The present application is directed to nucleic acid molecules at least 90%, 95%, 96%, 97%, 98% or 99% identical to the nucleic acid sequence shown in FIG. 1 (SEQ ID NO:1) or to the nucleic acid sequence of the deposited CDNA, irrespective of whether they encode a polypeptide having NAF-1 activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having NAF-1 activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having NAF-1 activity include, inter alia, (1) isolating the NAF-1 gene or allelic variants thereof in a CDNA library; (2) in situ hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the NAF-1 gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); and Northern Blot analysis for detecting NAF-1 mRNA expression in specific tissues.

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United States Patent 5,968,780
Fan , et al. October 19, 1999

This application claims benefit of 35 U.S.C. section 119(e) based on copending U.S. Provisional Application Serial No. 60/038,829, filed Feb. 6, 1997, which is hereby incorporated herein by reference.

1. An isolated nucleic acid molecule comprising a first polynucleotide sequence 95% or more identical to a second polynucleotide sequence selected from the group consisting of:
(a) a polynucleotide sequence encoding amino acids -26 to 485 of SEQ ID NO:2;
(b) a polynucleotide sequence encoding amino acids -25 to 485 of SEQ ID NO:2;
(c) a polynucleotide sequence encoding amino acids 1 to 485 of SEQ ID NO:2; and
(d) a polynucleotide sequence complementary to any of the polynucleotide sequences in (a), (b) or (c) above;
wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of the second polynucleotide sequence and that allows gaps of up to 5% of the total number of nucleotides of said nucleotide sequence.

The DCDGF protein of the present invention shares sequence homology with the translation product of the insect Sarcophaga perigrina (flesh fly) mRNA for Insect-Derived Growth Factor (IDGF) (see FIG. 2; SEQ ID NO:3). Thus, the complete DCDGF amino acid sequence of SEQ ID NO:2 shares about 38.0% identity and about 58.2% similarity with the amino acid sequence encoded by the insect mRNA for IDGF (Homma et al., supra, which can be accessed on GenBank as Accession No. D83125), as determined by analysis with Bestfit (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711) using the default parameters (see FIG. 2). The shared homology includes the conserved cysteines at positions 108 and 133 in SEQ ID NO:2, which also are conserved in the atrial gland granule-specific antigen (AGSA) of Aplysia californica, as reported by K. Homma et al., supra. IDGF is present throughout embryonic development and stimulates proliferation of embryonic insect cells and therefore is thought to be important in development of the insect from the fertilized egg. The homology between IDGF and DCDGF, as well as the facts that DCDGF is produced by dendritic cells, which activate T cells, and the gene for DCDGF has been mapped to a locus on chromosome 22 which is associated with DiGeorge Syndrome, all indicate

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involvement of DCDGF in early stages of human development and developmentally related pathologies including, for instance, DiGeorge Syndrome, as well as in immune system disorders, particularly relating to cellular immunity.

FIG. 2 shows the regions of identity between the amino acid sequences of the DCDGF protein (SEQ ID NO:2) and the translation product of the insect mRNA for IDGF (SEQ ID NO:3), determined by the computer program Bestfit (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711) using the default parameters.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1 or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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(excerpts from specification shown in italics)

United States Patent 5,985,614
Rosen , et al. November 16, 1999

This application claims the benefit of the filing date of provisional application No. 60/024,882 filed on Aug. 30, 1996, which is herein incorporated by reference.

5. The isolated nucleic acid molecule of claim 1, wherein said polypeptide sequence is (d).

6. The isolated nucleic acid molecule of claim 1, wherein said polypeptide sequence is (e).

7. The isolated nucleic acid molecule of claim 1, wherein the number of amino acid substitutions is one to three.

8. An isolated nucleic acid molecule comprising a first polynucleotide sequence at least 95% identical to a second polynucleotide sequence, wherein said second polynucleotide sequence is selected from the group consisting of:
(a) a polynucleotide sequence encoding amino acids -24 to 153 of SEQ ID NO:2;
(b) a polynucleotide sequence encoding amino acids -23 to 153 of SEQ ID NO:2;
(c) a polynucleotide sequence encoding amino acids 1 to 153 of SEQ ID NO:2;
(d) a polynucleotide sequence encoding the same amino acid sequence as encoded by the cDNA clone contained in ATCC Deposit No. 97662;
(e) a polynucleotide sequence encoding the mature interleukin-19 (IL-19) polypeptide having the amino acid sequence
encoded by the cDNA clone contained in ATCC Deposit No. 97662;
(f) a polynucleotide sequence encoding amino acids -5 to 4 of SEQ ID NO:2;
(g) a polynucleotide sequence encoding amino acids 64 to 82 of SEQ ID NO:2;
(h) a polynucleotide sequence encoding amino acids 115 to 125 of SEQ ID NO:2; and
(i) the complement of (a), (b), (c), (d), (e), (f), (g) or (h);
wherein % identity is calculated using BESTFIT with the parameters set such that % identity is calculated over the full length of said second polynucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in said second polynucleotide sequence are allowed.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1 or to the nucleotides sequence of the deposited cDNA clone can be determined

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conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. Bestfit uses the local homology algorithm of Smith and Waterman (Advances in Applied Mathematics 2: 482-489, 1981) to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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United States Patent 5,998,171
Yu , et al. December 7, 1999

This application claims priority benefit to U.S. application Ser. No. 60/024,058, filed Aug. 16, 1996, which disclosure is herein incorporated by reference.

90. An isolated polynucleotide comprising a first nucleotide sequence 95% or more identical to a second nucleotide sequence selected from the group consisting of:
(a) a nucleotide sequence encoding amino acids 1 to 169 of SEQ ID NO:2;
(b) a nucleotide sequence encoding amino acids 2 to 169 of SEQ ID NO:2; and
(c) a nucleotide sequence encoding a polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97640;
wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of said second nucleotide sequence and that allow gaps of up to 5% of the total number of nucleotides of said second nucleotide sequence.

As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98%, or 99% identical to, for instance, the nucleotide sequence shown in FIGS. 1A-1B or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the BESTFIT program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). BESTFIT uses the local homology algorithm of Smith and Waterman, Adv. Appl. Math. 2:482-489 (1981), to find the best segment of homology between two sequences. When using BESTFIT or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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United States Patent 6,011,012
Ni , et al. January 4, 2000

The present application is a continuation-in-part application of co-pending U.S. patent application Ser. No. 08/461,030, filed Jun. 5, 1995.

1. An isolated polypeptide having cysteine protease inhibiting activity comprising an amino acid sequence selected from the group consisting of:
(a) the amino acid sequence no of SEQ ID NO:2 wherein n is any integer 1-35 and c is any integer 143-149;
(b) amino acid sequence at least 95% identical to the amino acid sequence of (a) as determined by the Bestfit computer program using default parameters;
(c) the amino acid sequence of a fragment of SEQ ID NO:2;
(d) an amino acid sequence at least 95% identical to the amino acid sequence of (c) as determined by the Bestfit computer program using default parameters;
(e) the amino acid sequence of a fragment of the polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97156; and
(f) an amino acid sequence at least 95% identical to the amino acid sequence of (e) as determined by the Bestfit computer program using default parameters.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1 or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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United States Patent 6,027,916
Ni , et al. February 22, 2000

This application claims the benefit of the filing date of provisional application 60/028,093 filed on Oct. 9, 1996, which is herein incorporated by reference.

1. An isolated nucleic acid molecule comprising a polynucleotide which encodes an amino acid sequence having at least 95% identity to an amino acid sequence selected from the group consisting of:
(a) amino acids 1 to 311 of SEQ ID NO:4;
(b) amino acids 2 to 311 of SEQ ID NO:4;
(c) amino acids 1 to 200 of SEQ ID NO:8;
(d) amino acids 2 to 200 of SEQ ID NO:8;
(e) the human Galectin 9 amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97733; and
(f) the human Galectin 10SV amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97734;
wherein said 95% identity is determined using the Bestfit program having parameters set such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIGS. 1, 2A-2B, 3A-3B, or 4A-4B (SEQ ID NOs: 1, 3, 5, or 7) or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981)), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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As a practical matter, whether any particular polypeptide is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in FIGS. 1, 2A-2B, 3A-3B, or 4A-4B (SEQ ID NOs:2, 4, 6, or 8, respectively) or to the amino acid sequence encoded by one of the deposited cDNA clones (ATCC Deposit Numbers 97732, 97733 and 97734) can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

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United States Patent 6,028,169
Kreider , et al. February 22, 2000

This application claims benefit of the filing date of provisional application 60/042,269 filed Mar. 31, 1997, which is herein incorporated by reference.

1. An isolated polypeptide selected from the group consisting of:
(a) a polypeptide comprising the amino acid sequence of residue 4 to residue m in SEQ ID NO:2, wherein m is any one of residues 48-93 of SEQ ID NO:2, and wherein said polypeptide inhibits the Chemokine Receptor-3 (CCR3) signaling pathway;
(b) a polypeptide comprising the amino acid sequence of (a) except for one or more conservative amino acid substitutions, wherein said polypeptide inhibits the Chemokine Receptor-3 (CCR3) signaling pathway; and
(c) a polypeptide comprising a sequence at least 80% identical to the amino acid sequence of (a), wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the fall length of sequence (a) and that allow gaps in homology of up to 20% of the total number of residues in sequence (a), and wherein said polypeptide inhibits the Chemokine Receptor-3 (CCR3) signaling pathway.

FIG. 2 illustrates a comparison of the amino acid sequence homology between the polypeptide of the present invention with human MCP-1 (SEQ ID NO:5). Ck.beta.-6 shows 36% identity and 52% similarity with human MCP-1 as determined by the computer program Bestfit.

The polynucleotide of this invention was discovered from an activated monocyte cDNA library. It contains an open reading frame encoding a protein of approximately 119 amino acids in length of which the first 26 amino residues comprise a putative leader sequence. The mature protein therefore is predicted to be 93 amino acids in length. It is structurally related to mouse monocyte chemotactic protein-1 (MCP-1 or JE, sequence not shown), and human MCP-1 (SEQ ID NO:5) showing 36% identity, and 52% simlarity over the entire human MCP-1 protein sequence as determined by the computer program Bestfit (shown in FIG. 2). The polypeptide contains all four cysteine residues that occur in all chemokines in a characteristic motif. The spacing between these cysteines is conserved compared with the human MCP-1 and murine MCP-1/JE which strongly suggests that the new gene is a chemokine.

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As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1, or to the nucleotide sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2: 482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in FIG. 1 (SEQ ID NO:2) or to the amino acid sequence encoded by the deposited cDNA clone can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the fall length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

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United States Patent 6,096,515
Crabtree , et al. August 1, 2000

Filed: March 9, 1998

12. The isolated polynucleotide of claim 1, which encodes a polypeptide comprising an amino acid sequence that is at least 90% identical to 20 or more consecutive amino acids of the sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

14. The isolated polynucleotide of claim 1, which encodes a polypeptide comprising a Rel Similarity Region having an amino acid sequence which is at least about 73% identical to the amino acid sequence set forth in SEQ ID NO: 51, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

18. An isolated polynucleotide encoding a polypeptide comprising an amino acid sequence which is at least 90% identical to 20 or more consecutive amino acids of the amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

28. An isolated polynucleotide comprising a nucleotide sequence which is at least 73% identical to the nucleotide sequence set forth in SEQ ID NO: 45, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

29. The isolated polynucleotide of claim 28, comprising a nucleotide sequence which is at least about 90% identical to the nucleotide sequence set forth in SEQ ID NO: 45, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2: 482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48: 443, by the search for similarity method of Pearson and Lipman (1988) Proc. Natl.

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(excerpts from specification shown in italics)

Acad. Sci. (U.S.A.) 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected. The term "sequence identity" means that two polynucleotide sequences are identical (i.e., on a nucleotide-by-nucleotide basis) over the window of comparison.

As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or more (e.g., 99 percent sequence identity).

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

United States Patent 6,130,079
Ni , et al. October 10, 2000

This application claims the benefit of the filing date of provisional application Ser. No. 60/033,868 filed on Dec. 20, 1996, which is herein incorporated by reference.

1. An isolated polynucleotide comprising a nucleotide sequence encoding an amino acid sequence at least 95% identical to amino acids 2 to 199 of SEQ ID NO:2,
wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of amino acids 2 to 199 of SEQ ID NO:2 and that allow gaps of up to 5% of the total number of residues in amino acids 2 to 199 of SEQ ID NO:2;
wherein said polynucleotide encodes a polypeptide which either induces apoptosis or generates antibody that binds the full length RAIDD protein

4. The isolated polynucleotide of claim 1, wherein said amino acid sequence is at least 95% identical to amino acids 1 to 199 of SEQ ID NO:2;
wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of amino acids 1 to 199 of SEQ ID NO:2 and that allow gaps of up to 5% of the total number of residues in amino acids 1 to 199 of SEQ ID NO:2.

17. The isolated polynucleotide of claim 15, wherein said amino acid sequence is at least 95% identical to the complete amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97824;
wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of the complete amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97824 and that allow gaps of up to 5% of the total number of residues of the complete amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97824.

70. An isolated polynucleotide comprising a nucleotide sequence encoding an amino acid sequence at least 95% identical to a reference amino acid sequence selected from the group consisting of:
(a) amino acids 8 to 80 of SEQ ID NO:2;
(b) amino acids 123 to 194 of SEQ ID NO:2;
(c) amino acids 1 to 117 of SEQ ID NO:2; and

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(d) amino acids 95 to 199 of SEQ ID NO:2;
wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of the reference amino acid sequence and that allow gaps of up to 5% of the total number of residues of the reference amino acid sequence;
wherein said polynucleotide encodes a polypeptide which either induces apoptosis or generates antibody that binds the full length RAIDD protein.

As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98% or 99% identical to those described above can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

United States Patent 6,143,498
Olsen , et al. November 7, 2000

This application claims the benefit of the filing date of provisional application Ser. No. 60/046,415 filed on May 14, 1997, which is herein incorporated in its entirety.

1. An isolated polynucleotide comprising a nucleic acid at least 95% identical to a reference nucleic acid encoding amino acids 1 to 41 of SEQ ID NO:2, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference nucleic acid and that allow gaps of up to 5% of the total number of nucleotides of said reference nucleic acid.

15. An isolated polynucleotide comprising a nucleic acid at least 95% identical to a reference nucleic acid encoding the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97982, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference nucleic acid and that allow gaps of up to 5% of the total number of nucleotides of said reference nucleic acid.

25. An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence at least 95% identical to amino acids 1 to 41 of SEQ ID NO:2 (the reference sequence), wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference sequence and that allow gaps of up to 5% of the total number of residues of said reference sequence.

36. An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence at least 95% identical to the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97982 (the reference sequence), wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference sequence and that allow gaps of up to 5% of the total number of residues of said reference sequence.

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As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in SEQ ID NO: 1 or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2: 482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

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Claims and specification of 27 U.S. Patents reciting "percent homology" or "BESTFIT" in claims
(excerpts from specification shown in italics)

United States Patent 6,150,099
Crabtree , et al. November 21, 2000

This application is a continuation application of Ser. No. 08/260,174 filed on Jun. 13, 1994, which is a continuation-in-part of U.S. Ser. No. 08/124,981 filed Sep. 20, 1993 (U.S. Pat. No. 5,837,840) which is a continuation-in-part of U.S. Ser. No. 07/749,385, filed Aug. 22, 1991 (U.S. Pat. No. 5,989,810).

5. The method of claim 1, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% identical to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights

16. The method of claim 15, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% similar to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

21. The method of claim 20, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% similar to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

25. The method of claim 23, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% identical to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin (genetics Software Package Release 7.0, using default gap weights.

29. The method of claim 27, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% identical to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

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35. The method of claim 33, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least about 80% identical to an amino acid sequence set forth in SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

38. A method for identifying a compound which modulates the activity of an NF-AT polypeptide, comprising
(i) contacting an isolated NF-AT polypeptide or portion thereof sufficient for interacting with a molecule, with the molecule and a compound in conditions under which, but for the presence of the compound, the NF-AT polypeptide or portion thereof and the molecule interact, wherein the NF-AT polypeptide comprises at least 25 amino acids having an amino acid sequence which is at least 80% identical to an amino acid sequence of SEQ ID NO: 38, wherein the percent identity is determined with the algorithm (GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights; and
(ii) determining the level of interaction between the NF-AT polypeptide or portion thereof and the molecule in the presence relative to the absence of the compound, such that a difference in the level of interaction between the NF-AT polypeptide or portion thereof and the molecule in the presence relative to the absence of the compound indicates that the compound modulates the activity of an NF-AT polypeptide.

Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2: 482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48: 443, by the search for similarity method of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. (U.S.A.) 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected.

As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or

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more (e.g., 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

Additionally, computerized comparison of sequences shown in FIG. 1 to existing sequence databases can identify sequence motifs and structural conformations found in other proteins or coding sequences that indicate similar domains of the NF-AT.sub.c protein. For example but not for limitation, the programs GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package (Genetics computer Group, 575 Science Dr., Madison, Wis.) can be used to identify sequences in databases, such as GenBank/EMBL, that have regions of homology with a NF-AT.sub.c sequences. Such homologous regions are candidate structural or functional domains. Alternatively, other algorithms are provided for identifying such domains from sequence data.

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(excerpts from specification shown in italics)

United States Patent 6,171,781
Crabtree , et al. January 9, 2001

This application is a continuation-in-part of application Ser. No. 08/260,174, entitled "NF-AT Polypeptides and Polynucleotides", filed Jun. 13, 1994, which is a continuation-in-part of application Ser. No. 08/124,981, entitled "NF-AT Polypeptides and Polynucleotides", filed Sep. 20, 1993, U.S. Pat. No. 5,837,840. These applications are hereby incorporated by referenced herein.

42. A method for identifying a compound which modulates translocation of an NF-AT polypeptide across the nuclear membrane of a cell by binding of the compound to the NF-AT polypeptide, comprising
(i) contacting test compounds with an NF-AT polypeptide, or portion thereof, wherein the NF-AT polypeptide comprises at least 25 contiguous amino acids having an amino acid sequence which is at least 80% identical to an amino acid sequence of SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights;
(ii) identifying those test compounds which bind to the NF-AT polypeptide; and determining which of the test compounds so identified modulates translocation of an NF-AT polypeptide across the nuclear membrane of a cell.

60. A method for identifying a compound which promotes or inhibits translocation of an NF-AT polypeptide across the nuclear membrane of a cell, comprising

(i) providing a polypeptide complex comprising a nuclear localization sequence (NLS) of an NF-AT polypeptide and a portion of an NF-AT polypeptide which binds to said NLS, wherein the NF-AT polypeptide comprises at least 25 contiguous amino acids having an amino acid sequence which is at least 80% identical to an amino acid sequence of SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights;
(ii) contacting the polypeptide complex with test compounds and determining whether a test compound modulates the binding of the NLS to the portion of an NF-AT polypeptide which binds to said NLS; and

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(iii) determining which of the test compounds so identified promotes or inhibits translocation of an NF-AT polypeptide across the nuclear membrane of a cell.

Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2: 482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48: 443, by the search for similarity method of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. (U.S.A.) 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected.

As applied to polypeptides, a degree of identity of amino acid sequences is a function of the number of identical amino acids at positions shared by the amino acid sequences. A degree of homology or similarity of amino acid sequences is a function of the number of amino acids, i.e. structurally related, at positions shared by the amino acid sequences. An "unrelated" or "non-homologous" sequence shares less than 40% identity, though preferably less than 25% identity, with one of the NF-ATc sequences of the present invention. The term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or more (e.g., 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

Additionally, computerized comparison of sequences shown in FIG. 1 to existing sequence databases can identify sequence motifs and structural conformations found in other proteins or coding sequences that indicate similar domains of the NF-AT.sub.c protein. For example but not for limitation, the programs GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package (Genetics Computer Group, 575 Science Dr., Madison, Wis.) can be used to identify sequences in databases, such as GenBank/EMBL, that have regions of homology with a NF-AT.sub.c sequences. Such homologous regions are candidate structural or functional domains.

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(excerpts from specification shown in italics)

United States Patent 6,171,816
Yu , et al. January 9, 2001

This application claims priority benefit to U.S. application Ser. No. 60/024,347, filed Aug. 23, 1996, which disclosure is herein incorporated by reference.

86. An isolated polynucleotide comprising a nucleic acid at least 95% identical to a reference nucleic acid encoding amino acids 1 to 155 of SEQ ID NO:2, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference nucleic acid and that allow gaps of up to 5% of the total number of nucleotides of said reference nucleic acid.

100. An isolated polynucleotide comprising a nucleic acid at least 95% identical to a reference nucleic acid encoding the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97641, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference nucleic acid and that allow gaps of up to 5% of the total number of nucleotides of said reference nucleic acid.

111. An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence at least 95% identical to a reference amino acid sequence consisting of amino acids 1 to 155 of SEQ ID NO:2, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference amino acid sequence and that allow gaps of up to 5% of the total number of residues of said reference amino acid sequence.

124. An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence at least 95% identical to a reference amino acid sequence consisting of the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97641, wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said reference amino acid sequence and that allow gaps of up to 5% of the total number of residues of said reference amino acid sequence.

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As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5 or to the nucleotides sequence of the deposited cDNA clones can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

As a practical matter, whether any particular polypeptide is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6 or to the amino acid sequence encoded by deposited cDNA clones can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

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(excerpts from specification shown in italics)

United States Patent 6,174,532
Campo , et al. January 16, 2001

Appl. No.: 817548
Filed: May 12, 1997
PCT Filed: October 6, 1995
PCT NO: PCT/GB95/02372
371 Date: May 12, 1997
102(e) Date: May 12, 1997
PCT PUB.NO.: WO96/11273
PCT PUB. Date: April 18, 1996

1. An immunogenic peptide for the treatment of papillomavirus infection, wherein the peptide is: (a) a peptide from 10-30 amino acid residues in length having a sequence corresponding to a sequence from the N terminal amino acids 11-200 of papillomavirus L2 protein, (b) a peptide of 10-30 amino acid residues in length with at least 30% identity with the sequence from (a) as determined using the BESTFIT program, or (c) a peptide as defined in either (a) or (b) which is conjugated or fused to a protein or peptide other than a papillomavirus L2 protein or peptide.

Naturally, the skilled addressee will appreciate that there are computer programs available in the art which are able to make alignments between different amino acid sequences. An example of such a program is BESTFIT of TRANSLATE in the Genetic Computer Group (University of Wisconsin) package.

Examples of at least 10 amino acid residue long peptide sequences and of 14 amino acid long peptide sequences which can be optimally aligned using an appropriate computer program as described above (e.g. Bestfit of Translate) and are capable of being included in a peptide, polypeptide or protein format capable of an immunogenic potential include HPV-18, HPV-16, HPV-11 and HPV-6 as shown hereinbelow:

THR ASP PRO SER ILE VAL THR LEU ILE GLU HPV-18 (SEQ ID NO.4)
SER ASP PRO SER ILE VAL SER LEU VAL GLU HPV-16 (SEQ ID NO.5)
SER ASP PRO SER ILE VAL SER LEU ILE GLU HPV-11 (SEQ ID NO.6)
SER ASP PRO SER ILE VAL SER LEU ILE GLU HPV-6 (SEQ ID NO.7)
SER ASP PRO SER ILE VAL SER LEU ILE GLU CONSENSUS (SEQ ID NO.8)

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HPV-18 ILE THR SER ALA GLY THR THR THR PRO ALA VAL LEU ASP ILE (SEQ ID NO.9)
HPV-16 ILE THR THR SER THR ASP THR THR PRO ALA ILE LEU ASP ILE (SEQ ID NO.10)
HPV-11 ILE THR SER SER GLU SER THR THR PRO ALA ILE LEU ASP VAL (SEQ ID NO.11)
HPV-6 ILE THR SER SER GLU THR THR THR PRO ALA ILE LEU ASP VAL (SEQ ID NO.12)
CONSENSUS
ILE THR SER SER GLU THR THR THR PRO ALA ILE LEU ASP VAL (SEQ ID NO.13)

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(excerpts from specification shown in italics)

United States Patent 6,242,566
Godfrey ,et al. June 5, 2001

Filed: February 10, 1994

28. An isolated ACT-4-L ligand polypeptide comprising an amino acid sequence that is a variant of the amino acid sequence of the extracellular domain of the ACT-4-L polypeptide shown in FIG. 10 (SEQ ID NO: 4), said variant having at least about 80% sequence identity to the amino acid sequence of the extracellular domain, said extracellular domain having an amino terminus of amino acid 51 of the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4) and a carboxyl terminus of amino acid 183 of the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4), said polypeptide having the ability to bind specifically to the ACT-4-h-1 receptor shown in FIG. 5 (SEQ ID NO: 2).

34. The isolated ACT-4-L ligand polypeptide of claim 28 wherein said sequence identity is determined by use of a BESTFIT homology algorithm with default gap weights.

35. An isolated ACT-4-L ligand soluble polypeptide comprising an amino acid sequence that has at least about 80% sequence identity to the amino acid sequence of the extracellular domain of the ACT-4-L polypeptide shown in FIG. 10 (SEQ ID NO: 4), said sequence identity being determined by use of a BESTFIT homology algorithm with default gap weights, said extracellular domain having an amino terminus of amino acid 51 of the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4) and a carboxyl terminus of amino acid 183 of the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4), said soluble polypeptide having the ability to bind specifically to the ACT-4-h-1 receptor shown in FIG. 5 (SEQ ID NO: 2).

37. An isolated variant ACT-4-L ligand polypeptide comprising an amino acid sequence that is a variant of the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4) and which has at least about 80% sequence identity to the amino acid sequence shown in FIG. 10 (SEQ ID NO: 4), said sequence identity being determined by use of a BESTFIT homology algorithm with default gap weights, said polypeptide having the ability to bind specifically to the ACT-4-h-1 receptor shown in FIG. 5 (SEQ ID NO: 2).

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Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith & Waterman, Appl. Math. 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, J. Mol. Biol. 48:443 (1970), by the search for similarity method of Pearson & Lipman, Proc. Natl. Acad. Sci. (USA) 85:2444 (1988), by computerized implementations of these algorithms (FASTDB (Intelligenetics), BLAST (National Center for Biomedical Information) or GAP, BESTFIT, FASTA, and TFASTA (Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.)), or by inspection, and the best alignment (i.e., resulting in the highest percentage of sequence similarity over the comparison window) generated by the various methods is selected.

As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs BLAZE (Intelligenetics) GAP or BESTFIT using default gap weights, share at least 70 percent or 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or more (e.g., 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

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United States Patent 6,261,801
Wei , et al. July 17, 2001

This application claims benefit of 35 U.S.C. section 119(e) based on U.S. Provisional Application Ser. No. 60/035,496, filed Jan. 14, 1997 and No. 60/054,885, filed Aug. 7, 1997.

1. An isolated nucleic acid molecule comprising a first polynucleotide sequence 95% or more identical to a second polynucleotide sequence selected from the group consisting of:
(a) a polynucleotide sequence encoding amino acids -26 to 233 of SEQ ID NO:2;
(b) a polynucleotide sequence encoding amino acids -25 to 233 of SEQ ID NO:2;
(c) a polynucleotide sequence encoding amino acids 1 to 233 of SEQ ID NO:2; and
(d) a polynucleotide sequence complementary to any of the polynucleotide sequences in (a), (b) or (c) above;
wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of the second polynucleotide sequence and that allows gaps of up to 5% of the total number of nucleotides of said nucleotide sequence.

21. An isolated nucleic acid molecule comprising a first polynucleotide sequence 95% or more identical to a second polynucleotide sequence selected from the group consisting of:
(a) a polynucleotide sequence encoding a TRID (TRAIL receptor without intracellular domain) polypeptide having the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97798;
(b) a polynucleotide sequence encoding the mature TRID polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97798; and
(c) a polynucleotide sequence complementary to any of the polynucleotide sequences in (a) or (b) above;
wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of the second polynucleotide sequence and that allows gaps of up to 5% of the total number of nucleotides of said nucleotide sequence.

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38. An isolated nucleic acid molecule comprising a first polynucleotide sequence 95% or more identical to a second polynucleotide sequence selected from the group consisting of:
(a) a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of residues m to 233 of SEQ ID NO:2, where m is an integer in the range of -26 to 27;
(b) a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of residues -26 to x of SEQ ID NO:2, where x is an integer in the range of 123 to 233; and
(c) a polynucleotide sequence encoding a polypeptide having the amino acid sequence consisting of residues m to x of SEQ ID NO2, m and x are defined in (a) and (b) above; wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of the second polynucleotide sequence and that allows gaps of up to 5% of the total number of nucleotides of said nucleotide sequence.

137. An isolated nucleic acid molecule comprising a first polynucleotide sequence 90% or more identical to a second polynucleotide sequence selected from the group consisting of:
(a) a polynucleotide sequence encoding a TRID (TRAIL receptor without intracellular domain) polypeptide having the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97798;
(b) a polynucleotide sequence encoding the mature TRID polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97798; and
(c) a polynucleotide sequence complementary to any of the polynucleotide sequences in (a) or (b) above; wherein percentage identity is determined using the BESTFIT program with parameters that calculate identity over the full length of the second polynucleotide sequence and that allows gaps of up to 10% of the total number of nucleotides of said nucleotide sequence.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in SEQ ID NO:1, or to the nucleotide sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics

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2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in SEQ ID NO:2, or to the amino acid sequence encoded by the deposited cDNA clone, can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in SEQ ID NO:2, or to the amino acid sequence encoded by the deposited cDNA clone, can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

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United States Patent 6,284,486
Olsen , et al. September 4, 2001

This application hereby claims priority benefit to U.S. Appl. Ser. No. 60/033,869, filed Dec. 20, 1996 and U.S. Appl. Ser. No. 60/037,388, filed Feb. 7, 1997, which are hereby incorporated by reference.

62. An isolated polynucleotide comprising a first nucleic acid 95% or more identical to a reference nucleic acid encoding an amino acid sequence selected from the group consisting of:
(a) amino acids -20 to 142 of SEQ ID NO:2;
(b) amino acids -19 to 142 of SEQ ID NO:2;
(c) amino acids 1 to 142 of SEQ ID NO:2;
(d) the amino acid sequence of the mature polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97825; and
(e) the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97825;
wherein percent identity is calculated using Bestfit with the parameters set such that percentage of identity is calculated over the full length of the reference nucleic acid and that gaps in homology of up to 5% of the total number of nucleotides in the reference nucleic acid are allowed.

67. An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence 95% or more identical to a reference amino acid sequence selected from the group consisting of:
(a) amino acids -20 to 142 of SEQ ID NO:2;
(b) amino acids -19 to 142 of SEQ ID NO:2;
(c) amino acids 1 to 142 of SEQ ID NO:2;
(d) the amino acid sequence of the mature polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97825; and
(e) the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97825;
wherein percent identity is calculated using Bestfit with the parameters set such that percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acids in the reference amino acid sequence are allowed.

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68. An isolated polynucleotide comprising a nucleic acid which is 95% or more identical to a reference nucleic acid, wherein said reference nucleic acid is selected from the group consisting of:
(a) nucleotides 80 to 505 of SEQ ID NO:1;
(b) nucleotides 23 to 505 of SEQ ID NO:1; and
(c) nucleotides 20 to 505 of SEQ ID NO:1;
wherein percent identity is calculated using Bestfit with the parameters set such that percentage of identity is calculated over the full length of the reference nucleic acid and that gaps in homology of up to 5% of the total number of nucleotides in the reference nucleic acid are allowed.

As a practical matter, whether any particular nucleic acid molecule is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in SEQ ID NO:1 or to the nucleotide sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2: 482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

As a practical matter, whether any particular polypeptide is at least 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence shown in SEQ ID NO:2 or to the amino acid sequence encoded by the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acid residues in the reference sequence are allowed.

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United States Patent 6,329,568
Gonsalves , et al. December 11, 2001

This application is a 371 of PCT/US94/01046 filed Jan. 27, 1994, which is a continuation of Ser. No. 08/010,410, filed Jan. 29, 1993, now abandoned.

23. An isolated DNA molecule comprising a nucleotide sequence having, over its entire length, above 80% similarity to the nucleotide sequence of SEQ. ID. No. 18, as measured using BESTFIT of the GCG sequence analysis software.

24. An isolated DNA molecule comprising a nucleotide sequence having, over its entire length, at least 80% similarity to the nucleotide sequence of SEQ. ID. No. 19, as measured using BESTFIT of the GCG sequence analysis software.

gene Com- Overall 53 K protein gene Intergenic 29 K protein
parisons.sup.a nt nt aa nt nt aa
B/ 76.4.sup.b 80.0 86.1 72.4 77.5 91.5(79.1)
CPNH1 (78.3).sup.c
B/L3 75.8 79.0 89.0(82.0) 76.4 78.0 91.1(79.9)
B/BL 76.3 -- -- 72.8 77.6 90.3(79.5)
B/I 63.0 -- -- -- 63.1 69.7(55.3)
CPNH1/L3 94.8 95.6 92.0(89.4) 89.2 96.8 99.6(98.5)
CPNH1/BL 96.4 -- -- 95.9 97.2 98.8(96.9)
CPNH1/I 62.7 -- -- -- 60.8 69.5(55.1)
L3/BL 95.1 -- -- 92.6 97.3 99.2(98.5)
L3/I 60.9 -- -- -- 60.9 69.5(55.1)
I/BL 61.7 -- -- -- 60.9 68.8(53.9)
.sup.a The partial or complete S RNA sequences of isolates TSWV-CPNH1 (2.916 kb), TSWV-L3 (2.837 kb), TSWV-BL (2.037 kb) and TSWV-I (1.144 kb) were used for comparisons with the S RNA sequence of the TSWV-B (3.049 kb).
.sup.b Percent similarities were calculated by Comparison of their nucleotide or predicted amino acid sequence using the program BESTFIT of the GCG Sequence analysis software package.
.sup.c Percent identity is in parenthesis.

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United States Patent 6,388,052
Crabtree , et al. May 14, 2002

This application is a continuation application of Ser. No. 08/260,174 filed on Jun. 13, 1994, now U.S. Pat. No. 6,197,925 which is a continuation-in-part of U.S. Ser. No. 08/124,981 filed Sep. 20, 1993 (now U.S. Pat. No. 5,837,840).

1. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to at least 20 consecutive amino acids of SEQ ID NO: 38, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

2. The isolated polypeptide of claim 1, comprising an amino acid sequence which is at least 95% identical to at least 20 consecutive amino acids of SEQ ID NO: 38, wherein the percent identity is determined with the algorithm CAP, BESTFIT or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

15. The isolated polypeptide of claim 1, comprising an amino acid sequence which is at least 90% identical to at least 20 consecutive amino acids of the Rel Similarity Domain set forth in SEQ ID NO: 51, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

17. The polypeptide of claim 1, which comprises a Rel Similarity domain having an amino acid sequence which is at least about 73% identical to the amino acid sequence set forth in SEQ ID NO: 51, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

18. The polypeptide of claim 17, which comprises a Rel Similarity domain having an amino acid sequence which is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO: 51, wherein the percent identity is determined with the algorithm GAP, BESTFIT, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

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Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2: 482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48: 443, by the search for similarity method of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. (U.S.A.) 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected.

As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or more (e.g., 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

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United States Patent 6,403,557
Greene , et al. June 11, 2002

This application is a continuation-in-part of, and claims the benefit of priority under 35 U.S.C. .sctn.120 to U.S. application Ser. No. 08/462,965, filed Jun. 5, 1995, now issued as U.S. Pat. No. 5,728,546 and PCT Application No. PCT/US095/07108, filed Jun. 5, 1995. This application also claims the benefit of priority under 35 U.S.C. .sctn.119(e) of U.S. Provisional Application Ser. Nos. 60/031,969 and 60/031,575, filed Nov. 27, 1996 and Dec. 4, 1996, respectively.

32. An isolated protein molecule comprising a first amino acid sequence having a least 95% identity to a second amino acid sequence selected from the group consisting of:
(a) amino acids +1 to +193 of SEQ ID NO:2;
(b) a mature portion of the protein encoded by the cDNA contained in ATCC Deposit No. 97148;
(c) amino acids -23 to +193 of SEQ ID NO:2; and
(d) the full length amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97148,
wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said second amino acid sequence and that allow for gaps of homology of up to 5% of the total number of amino acid residues in said second amino acid sequence.

43. An isolated protein molecule comprising a first amino acid sequence having at least 95% identity to a second amino acid sequence selected from the group consisting of:
(a) amino acids residues n to +193 of SEQ ID NO:2, wherein n is an integer in the range of -23 to +10;
(b) amino acids residues -22 to m of SEQ ID NO:2, wherein m is an integer in the range of +154 to +192;
(c) amino acids n to m of SEQ ID NO:2, wherein n is an integer in the range of -23 to +10 and m is an integer in the range of +154 to +192; and
(d) a polypeptide consisting of a portion of the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97148 wherein said portion excludes up to 33 amino acids from the amino terminus and up to 39 amino acids from the C-terminus of said complete amino acid sequence,

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wherein % identity is determined using the Bestfit program with parameters that calculate % identity over the full length of said second amino acid sequence and that allow for gaps in homology of up to 5% of the total number of amino acids residues in said second amino acid sequence.

As a practical matter, whether any particular nucleic acid molecule is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the nucleotide sequence shown in FIG. 1 or to the nucleotides sequence of the deposited cDNA clone can be determined conventionally using known computer programs such as the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). Bestfit uses the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981), to find the best segment of homology between two sequences. When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence according to the present invention, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

By "% similarity" for two polypeptides is intended a similarity score produced by comparing the amino acid sequences of the two polypeptides using the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711) and the default settings for determining similarity. Bestfit uses the local homology algorithm of Smith and Waterman (Advances in Applied Mathematics 2:482-489, 1981) to find the best segment of similarity between two sequences.

Appendix D
66 FR 1099, January 5, 2001
"Guidelines for Examination of Patent Application Under 35 U.S.C. 12, ¶1, "Written Description Requirement"

an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Similarly, Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered.

Once a *prima facie* showing of no specific and substantial credible utility has been properly established, the applicant bears the burden of rebutting it. The applicant can do this by amending the claims, by providing reasoning or arguments, or by providing evidence in the form of a declaration under 37 CFR 1.132 or a patent or a printed publication that rebuts the basis or logic of the *prima facie* showing. If the applicant responds to the *prima facie* rejection, the Office personnel should review the original disclosure, any evidence relied upon in establishing the *prima facie* showing, any claim amendments, and any new reasoning or evidence provided by the applicant in support of an asserted specific and substantial credible utility. It is essential for Office personnel to recognize, fully consider and respond to each substantive element of any response to a rejection based on lack of utility. Only where the totality of the record continues to show that the asserted utility is not specific, substantial, and credible should a rejection based on lack of utility be maintained.

If the applicant satisfactorily rebuts a *prima facie* rejection based on lack of utility under § 101, withdraw the § 101 rejection and the corresponding rejection imposed under § 112, first paragraph.

Dated: December 29, 2000.

Q. Todd Dickinson,

Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office.

[FR Doc. 01-322 Filed 1-4-01; 8:45 am]

BILLING CODE 3510-16-U

DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

[Docket No. 991027288-0264-02]

RIN 0651-AB10

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement

AGENCY: United States Patent and Trademark Office, Commerce.

ACTION: Notice.

SUMMARY: These Guidelines will be used by USPTO personnel in their review of patent applications for compliance with the "written description" requirement of 35 U.S.C. 112, ¶ 1. These Guidelines supersede the "Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 'Written Description' Requirement" that were published in the **Federal Register** at 64 FR 71427, Dec. 21, 1999, and in the Official Gazette at 1231 O.G. 123, Feb. 29, 2000. These Guidelines reflect the current understanding of the USPTO regarding the written description requirement of 35 U.S.C. 112, ¶ 1, and are applicable to all technologies.

DATES: The Guidelines are effective as of January 5, 2001.

FOR FURTHER INFORMATION CONTACT: Stephen Walsh by telephone at (703) 305-9035, by facsimile at (703) 305-9373, by mail to his attention addressed to United States Patent and Trademark Office, Box 8, Washington, DC 20231, or by electronic mail at "stephen.walsh@uspto.gov"; or Linda Therkorn by telephone at (703) 305-8800, by facsimile at (703) 305-8825, by mail addressed to Box Comments, Commissioner for Patents, Washington, DC 20231, or by electronic mail at "linda.therkorn@uspto.gov."

SUPPLEMENTARY INFORMATION: As of the publication date of this notice, these Guidelines will be used by USPTO personnel in their review of patent applications for compliance with the "written description" requirement of 35 U.S.C. 112, ¶ 1. Because these Guidelines only govern internal practices, they are exempt from notice and comment rulemaking under 5 U.S.C. 553(b)(A).

Discussion of Public Comments

Comments were received from 48 individuals and 18 organizations in response to the request for comments on the "Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 'Written Description' Requirement" published in the **Federal Register** at 64 FR 71427, Dec. 21, 1999, and in the Official Gazette at 1231 O.G. 123, Feb. 29, 2000. The written comments have been carefully considered.

Overview of Comments

The majority of comments favored issuance of final written description guidelines with minor revisions. Comments pertaining to the written description guidelines are addressed in detail below. A few comments addressed particular concerns with respect to the associated examiner training materials that are available for public inspection at the USPTO web site (www.uspto.gov). Such comments will be taken under advisement in the revision of the training materials; consequently, these comments are not specifically addressed below as they do not impact the content of the Guidelines. Several comments raised issues pertaining to the patentability of ESTs, genes, or genomic inventions with respect to subject matter eligibility (35 U.S.C. 101), novelty (35 U.S.C. 102), or obviousness (35 U.S.C. 103). As these comments do not pertain to the written description requirement under 35 U.S.C. 112, they have not been addressed. However, the aforementioned comments are fully addressed in the "Discussion of Public Comments" in the "Utility Examination Guidelines" Final Notice, which will be published at or about the same time as the present Guidelines.

Responses to Specific Comments

(1) *Comment:* One comment stated that the Guidelines instruct the patent examiner to determine the correspondence between what applicant has described as the essential identifying characteristic features of the invention and what applicant has claimed, and that such analysis will lead to error. According to the comment, the examiner may decide what applicant should have claimed and reject the claim for failure to claim what the examiner considers to be the invention. Another comment suggested that the Guidelines should clarify what is meant by "essential features of the invention." Another comment suggested that what applicant has identified as the "essential distinguishing characteristics" of the invention should be understood in terms of *Fiers* v. *Revel*, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993) ("Conception of a substance claimed *per se* without reference to a process requires conception of its structure, name,

formula, or definitive chemical or physical properties.").

Response: The suggestions have been adopted in part. The purpose of the written description analysis is to confirm that applicant had possession of what is claimed. The Guidelines have been modified to instruct the examiners to compare the scope of the invention claimed with the scope of what applicant has defined in the description of the invention. That is, the Guidelines instruct the examiner to look for consistency between a claim and what provides adequate factual support for the claim as judged by one of ordinary skill in the art from reading the corresponding written description.

(2) *Comment:* Two comments urge that *Regents of the University of California* v. *Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), is bad law and should not be followed by the USPTO because it conflicts with binding precedent, such as *Vas-Cath* v. *Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). *Response:* The final Guidelines are based on the Office's current understanding of the law and are believed to be fully consistent with binding precedent of the U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit. *Eli Lilly* is a precedential decision by the Court that has exclusive jurisdiction over appeals involving patent law. Accordingly, the USPTO must follow *Eli Lilly*. Furthermore, the USPTO does not view *Eli Lilly* as conflicting with *Vas-Cath*. *Vas-Cath* explains that the purpose of the written description requirement is to ensure that the applicant has conveyed to those of skill in the art that he or she was in possession of the claimed invention at the time of filing. *Vas-Cath*, 935 F.2d at 1563–64, 19 USPQ2d at 1117. *Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Thus, *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed.

(3) *Comment:* Several comments urged that the Guidelines do not recognize the inconsistency between the original claim doctrine and the written description requirement as set out in *Fiers* and *Eli Lilly*. On the other hand, another comment asserts that there is no strong presumption that an originally filed claim constitutes an adequate written description of the claimed subject matter. Several comments indicate that *in haec verba* support should be sufficient to comply with the written description requirement. Two comments urge that the concept of constructive reduction to practice upon filing of an application has been ignored. *Response:* As noted above, the USPTO does not find *Fiers* and *Eli Lilly* to be in conflict with binding precedent. An original claim may provide written description for itself, but it still must be an *adequate* written description which establishes that the inventor was in possession of the invention. The "original claim doctrine" is founded on cases which stand for the proposition that originally filed claims are part of the written description of an application as filed, and thus subject matter which is present only in originally filed claims need not find independent support in the specification. *See, e.g., In re Koller*, 613 F.2d 819, 824, 204 USPQ 702, 706 (CCPA 1980) (later added claims of similar scope and wording were adequately described by original claims); *In re Gardner*, 480 F.2d 879, 880, 178 USPQ 149, 149 (CCPA 1973) ("Under these circumstances, we consider the original claim in itself adequate 'written description' of the claimed invention. It was equally a 'written description' * * * whether located among the original claims or in the descriptive part of the specification."). However, as noted in the preceding comment, *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed. When the name of a novel chemical compound does not convey sufficient structural information about the compound to identify the compound, merely reciting the name is not enough to show that the inventor had possession of the compound at the time the name was written. The Guidelines indicate that there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, consistent with *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). In most cases, the statement that "an originally filed claim is its own written description," is borne out because the claim language conveys to others of skill in the art that the applicant was "in possession" of what is claimed. The Guidelines emphasize that the burden of proof is on the examiner to establish that a description as filed is not adequate and require the examiner to introduce sufficient evidence or technical reasoning to shift the burden of going forward with contrary evidence to the applicant.

(4) *Comment:* One comment stated that the Guidelines change the substance of the written description requirement to require some level of enablement. The comment stated that the *Eli Lilly* case should not be followed because its change in the quality of the description required is in conflict with precedent. Another comment suggested that to comply with the written description requirement, the description must both (i) demonstrate possession of the claimed invention by the applicant; and (ii) put the public in possession of the claimed invention. *Response:* As noted in the comment above, the USPTO is bound by the Federal Circuit's decision in *Eli Lilly*. The Guidelines have been revised to clarify that an applicant must provide a description of the claimed invention which shows that applicant was in possession of the claimed invention. The suggestion to emphasize that the written description requirement must put the public in possession of the invention has not been adopted because it removes much of the distinction between the written description requirement and the enablement requirement. Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention.

(5) *Comment:* One comment suggested that the Guidelines should provide examples of situations in which the written description requirement was met but the enablement requirement was not, and vice versa. Another comment stated that examiners often use enablement language in making

written description rejections. *Response:* The enablement and written description requirements are not coextensive and, therefore, situations will arise in which one requirement is met but the other is not. Federal Circuit case law demonstrates many circumstances where enablement or written description issues, but not both, were before the Court. These Guidelines are intended to clarify for the examining corps the criteria needed to satisfy the written description requirement. For examples applying these Guidelines to hypothetical fact situations, see the "Synopsis of Application of Written Description Guidelines" (examiner training materials available on-line at *http://www.uspto.gov/web/menu/written.pdf*). These examples, as well as the examination form paragraphs and instructions on their proper use, provide the appropriate language examiners should use in making written description rejections.

(6) *Comment:* One comment disagreed with the statement in an endnote that "the fact that a great deal more than just a process is necessary to render a product invention obvious means that a great deal more than just a process is necessary to provide written description for a product invention." The comment indicated that the statement is overly broad and inconsistent with the "strong presumption that an adequate written description of the claimed invention is present when the application is filed." As an extreme case, for example, for product-by-process claims, nothing else would be needed to provide the written description of the product. *Response:* The endnote has been clarified and is now more narrowly drawn. However, there is no *per se* rule that disclosure of a process is sufficient to adequately describe the products produced by the process. In fact, *Fiers* v. *Revel* and *Eli Lilly* involved special circumstances where the disclosure of a process of making and the function of the product alone did not provide an adequate written description for product claims. Even when a product is claimed in a product-by-process format, the adequacy of the written description of the process to support product claims must be evaluated on a case-by-case basis.

(7) *Comment:* Several comments urge that actual reduction to practice, as a method of satisfying the written description requirement by demonstrating possession, has been over-emphasized. *Response:* The Guidelines have been clarified to state that describing an actual reduction to practice is one of a number of ways to show possession of the invention. Description of an actual reduction to practice offers an important "safe haven" that applies to all applications and is just one of several ways by which an applicant may demonstrate possession of the claimed invention. Actual reduction to practice may be crucial in the relatively rare instances where the level of knowledge and level of skill are such that those of skill in the art cannot describe a composition structurally, or specify a process of making a composition by naming components and combining steps, in such a way as to distinguish the composition with particularity from all others. Thus, the emphasis on actual reduction to practice is appropriate in those cases where the inventor cannot provide an adequate description of what the composition is, and a definition by function is insufficient to define a composition "because it is only an indication of what the [composition] does, rather than what it is." *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406. *See also Amgen Inc.* v. *Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

(8) *Comment:* One comment asserts that the citation to *Pfaff* v. *Wells Electronics, Inc.*, 525 U.S. 55, 48 USPQ2d 1641 (1998) is inappropriate and should be deleted because *Pfaff* is concerned with § 102(b) on-sale bar, not written description. Another comment suggested that the Guidelines should provide an explanation of how the "ready for patenting" concept of *Pfaff* should be used in determining compliance with the written description requirement. *Response:* The Guidelines state the general principle that actual reduction to practice is not required to show possession of, or to adequately describe, a claimed invention (although, as noted in the previous comment, an actual reduction to practice is crucial in relatively rare instances). An alternative is to show that the invention described was "ready for patenting" as set out in *Pfaff*. For example, a *description* of activities that demonstrates the invention was "ready for patenting" satisfies the written description requirement. As *Wertheim* indicates, "how the specification accomplishes this is not material." 541 F.2d at 262, 191 USPQ at 96.

(9) *Comment:* One comment stated that the written description of a claimed DNA should be required to include the complete sequence of the DNA and claims should be limited to the DNA sequence disclosed. *Response:* Describing the complete chemical structure, *i.e.*, the DNA sequence, of a claimed DNA is one method of satisfying the written description requirement, but it is not the only method. *See Eli Lilly*, 119 F.3d at 1566, 43 USPQ2d at 1404 ("An adequate written description of a DNA . . . requires a precise definition, *such as* by structure, formula, chemical name, or physical properties." (emphasis added, internal quote omitted)). Therefore, there is no basis for a *per se* rule requiring disclosure of complete DNA sequences or limiting DNA claims to only the sequence disclosed.

(10) *Comment:* One comment stated that it is difficult to envision how one could provide a description of sufficient identifying characteristics of the invention without physical possession of a species of the invention, and thus this manner of showing possession should be considered as a way to show actual reduction to practice. *Response:* This suggestion has not been adopted. The three ways of demonstrating possession as set forth in the Guidelines are merely exemplary and are not mutually exclusive. While there are some cases where a description of sufficient relevant identifying characteristics will evidence an actual reduction to practice, there are other cases where it will not. *See, e.g., Ralston Purina Co.* v. *Far-Mar-Co, Inc.*, 772 F.2d 1570, 1576, 227 USPQ 177, 180 (Fed. Cir. 1985) (disclosure taken with the knowledge of those skilled in the art may be sufficient support for claims).

(11) *Comment:* One comment stated that the Guidelines should be revised to indicate that the test of disclosure of sufficiently detailed drawings should be expanded to include structural claiming of chemical entities. *Response:* The suggestion has been adopted.

(12) *Comment:* One comment stated that the Guidelines should reflect that an inventor is in possession of the invention when the inventor demonstrably has at least a complete conception thereof, and that factors and attributes which provide proof of written description should include evidence typically provided to prove a complete conception. *Response:* The suggestion has not been adopted because the conception analysis typically involves documentary evidence in addition to the description of the invention in the application as filed. However, it is acknowledged that if evidence typically provided to prove a complete conception is present in the specification as filed, it would be sufficient to show possession. The Federal Circuit has stated "[t]he conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession

of the complete mental picture of the invention." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994). As further noted by the Federal Circuit, in order to prove conception, "a party must show possession of every feature recited in the count, and that every limitation of the count must have been known to the inventor at the time of the alleged conception." *Coleman v. Dines*, 754 F.2d 353, 359, 224 USPQ 857, 862 (Fed. Cir. 1985).

(13) *Comment:* One comment indicated that a "possession" test does not appear in Title 35 of the U.S. Code and is not clearly stated by the Federal Circuit. Therefore, it is recommended that patent examiners be directed to use existing judicial precedent to make rejections of claims unsupported by a statutory written description requirement. *Response:* While the Federal Circuit has not specifically laid out a "possession" test, the Court has clearly indicated that possession is a cornerstone of the written description inquiry. *See, e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); *see also Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("[o]ne skilled in the art, reading the disclosure, must immediately discern the limitation at issue in the claims") (internal quote omitted). The possession test as set forth in the Guidelines is extrapolated from case law in a wide variety of technologies and is not intended to be limiting. Any rejections made by examiners will be made under 35 U.S.C. 112, ¶1, with supporting rationale. Final rejections are appealable if applicant disagrees and follows the required procedures to appeal.

(14) *Comment:* Two comments indicated that if the amino acid sequence for a polypeptide whose utility has been identified is described, then the question of possession of a class of nucleotides encoding that polypeptide can be addressed as a relatively routine matter using the understanding of the genetic code, and that the endnote addressing this issue should be revised. *Response:* The suggestion of these comments has been incorporated in the Guidelines and will be reflected in the training materials. However, based upon *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994), this does not mean that applicant was in possession of any particular species of the broad genus.

(15) *Comment:* One comment disagreed with an endnote which stated that a laundry list disclosure of moieties does not constitute a written description of every species in a genus. Specifically, the comment indicates that if the existence of a functional genus is adequately described in the specification, a laundry list of the species within that genus must satisfy the written description requirement. *Response:* The suggestion to revise the endnote will not be adopted. A lack of adequate written description problem arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosure. This was aptly demonstrated in *In re Bell* and *In re Baird* where possession of a large genus did not put a person of ordinary skill in the art in possession of any particular species. *See also Purdue Pharma*, 230 F.3d at 1328, 56 USPQ2d at 1487 (because the original specification did not disclose the later claimed concentration ratio was a part of the invention, the inventors cannot argue that they are merely narrowing a broad invention).

(16) *Comment:* One comment suggested that in the majority of cases, a single species will support a generic claim, and that the Guidelines should emphasize this point. *Response:* The suggestion has been adopted to a limited degree. The Guidelines now indicate that a single species may, in some instances, provide an adequate written description of a generic claim when the description of the species would evidence to one of ordinary skill in the art that the invention includes the genus. Note, however, *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 47 USPQ2d 1829 (Fed. Cir. 1998), where the species in the parent application was held not to provide written description support for the genus in the child application.

(17) *Comment:* One comment asserted that the Guidelines should focus on the compliance of the claims, not the specification, with the written description requirement. *Response:* This suggestion will not be adopted. "The specification shall contain a written description of the invention." 35 U.S.C. 112. The claims are part of the specification. *Id.*, ¶ 2. If an adequate description is provided, it will suffice "whether located among the original claims or in the descriptive part of the specification." *In re Gardner*, 480 F.2d 879, 880, 178 USPQ 149 (CCPA 1973). The entire disclosure, including the specification, drawings, and claims, must be considered.

(18) *Comment:* One comment asserted that the Guidelines confuse "new matter," 35 U.S.C. 132, with the written description requirement, and that the same standard for written description should be applied to both original claims and new or amended claims. *Response:* The Guidelines indicate that for both original and amended claims, the inquiry is whether one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time the application was filed.

(19) *Comment:* One comment suggested that the second paragraph of the section pertaining to determining what the claim as a whole covers should be deleted because it relates more to compliance with § 112, second paragraph, than with the written description requirement. *Response:* This suggestion will not be adopted. The claims must be construed and all issues as to the scope and meaning of the claim must be explored during the inquiry into whether the written description requirement has been met. The concept of treating the claim as a whole is applicable to all criteria for patentability.

(20) *Comment:* One comment suggested a different order for the general analysis for determining compliance with the written description requirement, starting with reading the claim, then the specification, and then determining whether the disclosure demonstrates possession by the applicant. *Response:* This suggestion will not be adopted. The claims must be construed as broadly as reasonable in light of the specification and the knowledge in the art. *See In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Then the disclosure must be evaluated to determine whether it adequately describes the claimed invention, i.e., whether it conveys to a person having ordinary skill in the art that the applicant had possession of what he or she now claims.

(21) *Comment:* Several comments suggested that the Guidelines are unclear with regard to how the examiner should treat the transitional phrase "consisting essentially of." The comments also suggested that the endnote that explains "consisting essentially of" does not make clear how the use of this intermediate transitional language affects the scope of the claim. Several comments stated that the USPTO does not have legal authority to treat claims reciting this language as open (equivalent to "comprising"). Another comment suggested that the phrase "clear indication in the specification" be replaced with "explicit or implicit indication." *Response:* The transitional phrase "consisting essentially of" "excludes

ingredients that would 'materially affect the basic and novel characteristics' of the claimed composition." *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 412 (Fed. Cir. 1984). The basic and novel characteristics of the claimed invention are limited by the balance of the claim. *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 896 (CCPA 1963). However, during prosecution claims must be read broadly, consistent with the specification. *In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Thus, *for purposes of searching for and applying prior art in a rejection under 35 U.S.C. 102 or 103*, if the specification or the claims do not define the "basic and novel" properties of the claimed subject matter (or if such properties are in dispute), the broadest reasonable interpretation consistent with the specification is that the basic and novel characteristics are merely the presence of the recited limitations. *See, e.g., Janakirama-Rao*, 317 F.2d at 954, 137 USPQ at 895–96. This does not indicate that the intermediate transitional language is never given weight. Applicants may amend the claims to avoid the rejections or seek to establish that the specification provides definitions of terms in the claims that define the basic and novel characteristics of the claimed invention which distinguish the claimed invention from the prior art. When an applicant contends that additional steps or materials in the prior art are excluded by the recitation of 'consisting essentially of,' applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). The language used in the Guidelines is consistent with *PPG Industries Inc. v. Guardian Industries Corp.*, 156 F.3d 1351, 1355, 48 USPQ2d 1351, 1355 (Fed. Cir. 1998) ("PPG could have defined the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics.").

(22) *Comment:* One comment stated that the written description should "disclose the invention," including why the invention works and how it was developed. *Response:* This suggestion has not been adopted. An inventor does not need to know how or why the invention works in order to obtain a patent. *Newman v. Quigg*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989). To satisfy the enablement requirement of 35 U.S.C. 112, ¶1, an application must disclose the claimed invention in sufficient detail to enable a person of ordinary skill in the art to make and use the claimed invention. To satisfy the written description requirement of 35 U.S.C. 112, ¶ 1, the description must show that the applicant was in possession of the claimed invention at the time of filing. There is no statutory basis to require disclosure of why an invention works or how it was developed. "Patentability shall not be negatived by the manner in which the invention was made." 35 U.S.C. 103(a).

(23) *Comment:* One comment recommended that the phrases "emerging and unpredictable technologies" and "unpredictable art" be replaced with the phrase—inventions characterized by factors which are not reasonably predictable in terms of the ordinary skill in the art—. *Response:* The suggestion is adopted in part and the recommended phrase has been added as an alternative.

(24) *Comment:* One comment recommended that the phrase "conventional in the art" be replaced with—part of the knowledge of one of ordinary skill in the art—. *Response:* The suggestion is adopted in part and the recommended phrase has been added as an alternative. The standard of "conventional in the art" is supported by case law holding that a patent specification "need not teach, and preferably omits, what is well known in the art." *See Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534, 3 USPQ2d 1737, 1743 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). *See also Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 1382, 53 USPQ2d 1225, 1231 (Fed. Cir. 1999).

(25) *Comment:* One comment recommended that the Guidelines be amended to state that the appropriate skill level for determining possession of the claimed invention is that of a person of *ordinary* skill in the art. *Response:* The comment has not been adopted. The statutory language itself indicates that compliance with the requirements of 35 U.S.C. 112, ¶1, is judged from the standard of "any person skilled in the art." It is noted, however, that the phrases "one of skill in the art" and "one of ordinary skill in the art" appear to be synonymous. *See, e.g., Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow *persons of ordinary skill in the art* to recognize that [he or she] invented what is claimed.' Thus, § 112, ¶ 1, ensures that, as of the filing date, the inventor conveyed with reasonable clarity to *those of skill in the art* that he was in possession of the subject matter of the claims." (citations omitted, emphasis added)).

(26) *Comment:* One comment stated that an endnote misstates the relevant law in stating that, to show inherent written descriptive support for a claim limitation, the inherent disclosure must be such as would be recognized by a person of ordinary skill in the art. The comment recommended that the endnote be amended to delete the reference to recognition by persons of ordinary skill and to cite *Pingree v. Hull*, 518 F.2d 624, 186 USPQ 248 (CCPA 1975), rather than *In re Robertson*, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999). *Response:* The comment has not been adopted. Federal Circuit precedent makes clear that an inherent disclosure must be recognized by those of ordinary skill in the art. *See, e.g., Hyatt v. Boone*, 146 F.3d 1348, 1354–55, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998) ("[T]he purpose of the description requirement is 'to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him.' * * * Thus, the written description must include all of the limitations of the interference count, or the applicant must show that any absent text is necessarily comprehended in the description provided *and would have been so understood* at the time the patent application was filed." (emphasis added)). *See also Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1346, 54 USPQ2d 1915, 1917 (Fed. Cir. 2000) (The "application considered as a whole must convey to one of ordinary skill in the art, either explicitly or inherently, that [the inventor] invented the subject matter claimed * * *. See * * * *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (descriptive matter may be inherently present in a specification if one skilled in the art would necessarily recognize such a disclosure)").

(27) *Comment:* Several comments pointed out an inconsistency in the **Federal Register** Notice re: the Revised Interim Written Description Guidelines. The inconsistency concerned the treatment of claims directed to an isolated DNA comprising SEQ ID NO:1 wherein SEQ ID NO:1 is an expressed sequence tag. The comments contrasted paragraphs 34 and 35 of the Response to

Public Comments with the statement in the text of the Guidelines that a genus must be supported by a representative number of species (as analyzed in Example 7 of the training materials). *Response:* The USPTO acknowledges that there was an inconsistency. The Office notes that a claim reciting a nucleic acid comprising SEQ ID NO:1 may be subject to a rejection for lack of an adequate written description where particular identifiable species within the scope of the claim lack an adequate written description. The training materials as amended exemplify an appropriate analysis.

(28) *Comment:* One comment stated that the USPTO should respond to the issue of whether the U.S. is meeting its TRIPs obligations. This comment noted that the USPTO did not address an earlier comment regarding the "Interim Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement," 63 FR 32,639, June 15, 1998, which questioned whether the written description requirement is truly different from the enablement requirement, and indicated that such a requirement may be contrary to the TRIPs provisions of the World Trade Organization (Article 27.1). Article 27.1 requires WTO Members to, *inter alia*, make patents available, with limited exceptions, for products and processes in all fields of technology so long as those products and processes are new, involve an inventive step, and are capable of industrial application. The comment further suggested a response. *Response:* TRIPs Article 27 does not address what must be included in a patent application to allow WTO Member officials to determine whether particular inventions meet the standards for patentability established in that Article. TRIPs Article 29, which is more relevant to this comment, states that Members "shall require" patent applicants to disclose their invention "in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art." If the written description is not clear and complete, the applicant may not have been in possession of the invention. This may support both written description and enablement standards. In addition, Article 29 expressly authorizes Members to require patent applicants to disclose the best method the inventor knows at the time of filing an application for carrying out the invention.

(29) *Comment:* Two comments commended the USPTO for eliminating the Biotechnology Specific Examples in the Revised Interim Written Description Guidelines and providing separate training materials. One comment indicated a need to reconfirm the examples set forth in the interim Written Description Guidelines published in 1998. *Response:* The current training materials reflect the manner in which the USPTO interprets the Written Description Guidelines.

(30) *Comment:* Several comments addressed specific concerns about the examiner training materials. *Response:* The comments received with respect to the training materials will be taken under advisement as the Office revises the training materials in view of the revisions to the Guidelines. The specific comments will not be addressed herein as they do not impact the language of the Guidelines.

Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement

These "Written Description Guidelines" are intended to assist Office personnel in the examination of patent applications for compliance with the written description requirement of 35 U.S.C. 112, ¶ 1. This revision is based on the Office's current understanding of the law and public comments received in response to the USPTO's previous request for public comments on its Revised Interim Written Description Guidelines and is believed to be fully consistent with binding precedent of the U.S. Supreme Court, as well as the U.S. Court of Appeals for the Federal Circuit and its predecessor courts.

This revision does not constitute substantive rulemaking and hence does not have the force and effect of law. It is designed to assist Office personnel in analyzing claimed subject matter for compliance with substantive law. Rejections will be based upon the substantive law, and it is these rejections which are appealable. Consequently, any perceived failure by Office personnel to follow these Guidelines is neither appealable nor petitionable.

These Guidelines are intended to form part of the normal examination process. Thus, where Office personnel establish a *prima facie* case of lack of written description for a claim, a thorough review of the prior art and examination on the merits for compliance with the other statutory requirements, including those of 35 U.S.C. 101, 102, 103, and 112, is to be conducted prior to completing an Office action which includes a rejection for lack of written description. Office personnel are to rely on this revision of the Guidelines in the event of any inconsistent treatment of issues involving the written description requirement between these Guidelines and any earlier guidance provided from the Office.

I. General Principles Governing Compliance With the "Written Description" Requirement for Applications

The first paragraph of 35 U.S.C. 112 requires that the "specification shall contain a written description of the invention * * *." This requirement is separate and distinct from the enablement requirement.[1] The written description requirement has several policy objectives. "[T]he 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed."[2] Another objective is to put the public in possession of what the applicant claims as the invention.[3] The written description requirement of the Patent Act promotes the progress of the useful arts by ensuring that patentees adequately describe their inventions in their patent specifications in exchange for the right to exclude others from practicing the invention for the duration of the patent's term.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.[4] An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.[5] Possession may be shown in a variety of ways including description of an actual reduction to practice,[6] or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete,[7] or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.[8] A question as to whether a specification provides an adequate written description may arise in the context of an original claim which is not described sufficiently, a new or amended claim wherein a claim limitation has been added or removed, or a claim to entitlement of an earlier priority date or effective filing date under 35 U.S.C. 119, 120, or 365(c).[9] Compliance with the written description requirement is a question of

fact which must be resolved on a case-by-case basis.[10]

A. Original Claims

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed.[11] However, the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention.[12] The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art.[13] This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function.[14] A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.[15]

B. New or Amended Claims

The proscription against the introduction of new matter in a patent application [16] serves to prevent an applicant from adding information that goes beyond the subject matter originally filed.[17] Thus, the written description requirement prevents an applicant from claiming subject matter that was not adequately described in the specification as filed. New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement.[18] While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction.[19] Deposits made after the application filing date cannot be relied upon to support additions to or correction of information in the application as filed.[20]

Under certain circumstances, omission of a limitation can raise an issue regarding whether the inventor had possession of a broader, more generic invention.[21] A claim that omits an element which applicant describes as an essential or critical feature of the invention originally disclosed does not comply with the written description requirement.[22]

The fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed.[23]

II. Methodology for Determining Adequacy of Written Description

A. Read and Analyze the Specification for Compliance With 35 U.S.C. 112, ¶ 1

Office personnel should adhere to the following procedures when reviewing patent applications for compliance with the written description requirement of 35 U.S.C. 112, ¶ 1. The examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed;[24] however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims.[25] Consequently, rejection of an original claim for lack of written description should be rare. The inquiry into whether the description requirement is met is a question of fact that must be determined on a case-by-case basis.[26]

1. For Each Claim, Determine What the Claim as a Whole Covers

Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description.[27] The entire claim must be considered, including the preamble language [28] and the transitional phrase.[29] The claim as a whole, including all limitations found in the preamble,[30] the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement.[31]

The examiner should evaluate each claim to determine if sufficient structures, acts, or functions are recited to make clear the scope and meaning of the claim, including the weight to be given the preamble.[32] The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, ¶ 1, for lack of adequate written description. Limitations may not, however, be imported into the claims from the specification.

2. Review the Entire Application to Understand How Applicant Provides Support for the Claimed Invention Including Each Element and/or Step

Prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, the examiner should review the claims and the entire specification, including the specific embodiments, figures, and sequence listings, to understand how applicant provides support for the various features of the claimed invention.[33] The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed [34] and should include a determination of the field of the invention and the level of skill and knowledge in the art. Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification.[35]

3. Determine Whether There is Sufficient Written Description to Inform a Skilled Artisan That Applicant was in Possession of the Claimed Invention as a Whole at the Time the Application Was Filed

a. Original claims. Possession may be shown in many ways. For example, possession may be shown, *inter alia*, by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention.[36]

A specification may describe an actual reduction to practice by showing

that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.[37] Description of an actual reduction to practice of a biological material may be shown by specifically describing a deposit made in accordance with the requirements of 37 CFR 1.801 *et seq.*[38]

An applicant may show possession of an invention by disclosure of drawings[39] or structural chemical formulas[40] that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. The description need only describe in detail that which is new or not conventional.[41] This is equally true whether the claimed invention is directed to a product or a process.

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

(1) For each claim drawn to a single embodiment or species:[47]

(a) Determine whether the application describes an actual reduction to practice of the claimed invention.

(b) If the application does not describe an actual reduction to practice, determine whether the invention is complete as evidenced by a reduction to drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole.

(c) If the application does not describe an actual reduction to practice or reduction to drawings or structural chemical formula as discussed above, determine whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention.

(i) Determine whether the application as filed describes the complete structure (or acts of a process) of the claimed invention as a whole. The complete structure of a species or embodiment typically satisfies the requirement that the description be set forth "in such full, clear, concise, and exact terms" to show possession of the claimed invention.[48] If a complete structure is disclosed, the written description requirement is satisfied for that species or embodiment, and a rejection under 35 U.S.C. 112, ¶ 1, for lack of written description must not be made.

(ii) If the application as filed does not disclose the complete structure (or acts of a process) of the claimed invention as a whole, determine whether the specification discloses other relevant identifying characteristics sufficient to describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.[49]

Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.[50] Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. In most technologies which are mature, and wherein the knowledge and level of skill in the art is high, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention.[51] In contrast, for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession. For example, disclosure of only a method of making the invention and the function may not be sufficient to support a product claim other than a product-by-process claim.[52] Furthermore, disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention.[53]

Any claim to a species that does not meet the test described under at least one of (a), (b), or (c) must be rejected as lacking adequate written description under 35 U.S.C. 112, ¶ 1.

(2) For each claim drawn to a genus:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a), above), reduction to drawings (see (1)(b), above), or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see (1)(c), above).[54]

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus.[55] What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus.[56] Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces.[57] If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, ¶ 1.

b. New claims, amended claims, or claims asserting entitlement to the benefit of an earlier priority date or filing date under 35 U.S.C. 119, 120, or

365(c). The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims.[58] However, when filing an amendment an applicant should show support in the original disclosure for new or amended claims.[59] To comply with the written description requirement of 35 U.S.C. 112, ¶ 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c), each claim limitation must be expressly,[60] implicitly,[61] or inherently[62] supported in the originally filed disclosure.[63] Furthermore, each claim must include all elements which applicant has described as essential.[64]

If the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, ¶ 1, as lacking adequate written description, or in the case of a claim for priority under 35 U.S.C. 119, 120, or 365(c), the claim for priority must be denied.

III. Complete Patentability Determination Under All Statutory Requirements and Clearly Communicate Findings, Conclusions, and Their Bases

The above only describes how to determine whether the written description requirement of 35 U.S.C. 112, ¶ 1, is satisfied. Regardless of the outcome of that determination, Office personnel must complete the patentability determination under all the relevant statutory provisions of title 35 of the U.S. Code.

Once Office personnel have concluded analysis of the claimed invention under all the statutory provisions, including 35 U.S.C. 101, 112, 102, and 103, they should review all the proposed rejections and their bases to confirm their correctness. Only then should any rejection be imposed in an Office action. The Office action should clearly communicate the findings, conclusions, and reasons which support them. When possible, the Office action should offer helpful suggestions on how to overcome rejections.

A. For Each Claim Lacking Written Description Support, Reject the Claim Under Section 112, ¶ 1, for Lack of Adequate Written Description

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption.[65] The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.[66] In rejecting a claim, the examiner must set forth express findings of fact regarding the above analysis which support the lack of written description conclusion. These findings should:

(1) Identify the claim limitation at issue; and

(2) Establish a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. A general allegation of "unpredictability in the art" is not a sufficient reason to support a rejection for lack of adequate written description.

When appropriate, suggest amendments to the claims which can be supported by the application's written description, being mindful of the prohibition against the addition of new matter in the claims or description.[67]

B. Upon Reply by Applicant, Again Determine the Patentability of the Claimed Invention, Including Whether the Written Description Requirement Is Satisfied by Reperforming the Analysis Described Above in View of the Whole Record

Upon reply by applicant, before repeating any rejection under 35 U.S.C. 112, ¶ 1, for lack of written description, review the basis for the rejection in view of the record as a whole, including amendments, arguments, and any evidence submitted by applicant. If the whole record now demonstrates that the written description requirement is satisfied, do *not* repeat the rejection in the next Office action. If the record still does not demonstrate that the written description is adequate to support the claim(s), repeat the rejection under 35 U.S.C. 112, ¶ 1, fully respond to applicant's rebuttal arguments, and properly treat any further showings submitted by applicant in the reply. When a rejection is maintained, any affidavits relevant to the 112, ¶ 1, written description requirement,[68] must be thoroughly analyzed and discussed in the next Office action.

Dated: December 29, 2000.

Q. Todd Dickinson,

Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office.

Endnotes

[1] *See, e.g., Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991).

[2] *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977).

[3] *See Regents of the University of California* v. *Eli Lilly*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998).

[4] *See, e.g., Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. Much of the written description case law addresses whether the specification as originally filed supports claims not originally in the application. The issue raised in the cases is most often phrased as whether the original application provides "adequate support" for the claims at issue or whether the material added to the specification incorporates "new matter" in violation of 35 U.S.C. 132. The "written description" question similarly arises in the interference context, where the issue is whether the specification of one party to the interference can support the newly added claims corresponding to the count at issue, *i.e.*, whether that party can "make the claim" corresponding to the interference count. *See, e.g., Martin* v. *Mayer*, 823 F.2d 500, 503, 3 USPQ2d 1333, 1335 (Fed. Cir. 1987).

In addition, early opinions suggest the Patent and Trademark Office was unwilling to find written descriptive support when the only description was found in the claims; however, this viewpoint was rejected. *See In re Koller*, 613 F.2d 819, 204 USPQ 702 (CCPA 1980) (original claims constitute their own description); *accord In re Gardner*, 475 F.2d 1389, 177 USPQ 396 (CCPA 1973); *accord In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) (accord). It is now well accepted that a satisfactory description may be in the claims or any other portion of the originally filed specification. These early opinions did not address the quality or specificity of particularity that was required in the description, *i.e.*, how much description is enough.

[5] *Lockwood* v. *American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

[6] An application specification may show actual reduction to practice by describing testing of the claimed invention or, in the case of biological materials, by specifically describing a deposit made in accordance with 37 CFR 1.801 *et seq. See also Deposit of Biological Materials for Patent Purposes, Final Rule*, 54 FR 34,864 (August 22, 1989) ("The requirement for a specific identification is consistent with the description requirement of the first paragraph of 35 U.S.C. 112, and to provide an antecedent basis for the biological material which either has been or will be deposited before the patent is granted." *Id.* at 34,876. "The description must be sufficient to permit verification that the deposited biological material is in fact that disclosed. Once the

patent issues, the description must be sufficient to aid in the resolution of questions of infringement." *Id.* at 34,880.). Such a deposit is not a substitute for a written description of the claimed invention. The written description of the deposited material needs to be as complete as possible because the examination for patentability proceeds solely on the basis of the written description. *See, e.g., In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985). *See also* 54 FR at 34,880 ("As a general rule, the more information that is provided about a particular deposited biological material, the better the examiner will be able to compare the identity and characteristics of the deposited biological material with the prior art.").

[7] *Pfaff* v. *Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

[8] *See Amgen, Inc.* v. *Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

[9] A description requirement issue can arise for original claims (*see, e.g., Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398) as well as new or amended claims. Most typically, the issue will arise in the context of determining whether new or amended claims are supported by the description of the invention in the application as filed (*see, e.g., In re Wright*, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989)), whether a claimed invention is entitled to the benefit of an earlier priority date or effective filing date under 35 U.S.C. 119, 120, or 365(c) (*see, e.g., Tronzo* v. *Biomet, Inc.*, 156 F.3d 1154, 47 USPQ2d 1829 (Fed. Cir. 1998); *Fiers* v. *Revel*, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993); *In re Ziegler*, 992 F.2d 1197, 1200, 26 USPQ2d 1600, 1603 (Fed. Cir. 1993)), or whether a specification provides support for a claim corresponding to a count in an interference (*see, e.g., Fields* v. *Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1971)).

[10] *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991).

[11] *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims").

[12] See endnote 4.

[13] For example, consider the claim "A gene comprising SEQ ID NO:1." A determination of what the claim as a whole covers may result in a conclusion that specific structures such as a promoter, a coding region, or other elements are included. Although all genes encompassed by this claim share the characteristic of comprising SEQ ID NO:1, there may be insufficient description of those specific structures (*e.g.*, promoters, enhancers, coding regions, and other regulatory elements) which are also included.

[14] A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. For example, even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. *Cf. In re Bell*, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993), and *In re Deuel*, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995) (holding that a process could not render the product of that process obvious under 35 U.S.C. 103). The Federal Circuit has pointed out that under United States law, a description that does not render a claimed invention obvious cannot sufficiently describe the invention for the purposes of the written description requirement of 35 U.S.C. 112. *Eli Lilly*, 119 F.3d at 1567, 43 USPQ2d at 1405.

Compare Fonar Corp. v. *General Electric Co.*, 107 F.3d 1543, 1549, 41 USPQ2d 1801, 1805 (Fed. Cir. 1997) ("As a general rule, where software constitutes part of a best mode of carrying out an invention, description of such a best mode is satisfied by a disclosure of the functions of the software. This is because, normally, writing code for such software is within the skill of the art, not requiring undue experimentation, once its functions have been disclosed. * * * Thus, flow charts or source code listings are not a requirement for adequately disclosing the functions of software.").

[15] *See, e.g., Fujikawa* v. *Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("*If* n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); *Purdue Pharma L.P.* v. *Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors * * * considered the [] ratio to be part of their invention * * *. There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

[16] 35 U.S.C. §§ 132 and 251. *See also In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326 (CCPA 1981). *See* Manual of Patent Examining Procedure (MPEP) §§ 2163.06–2163.07 (7th Ed., Rev. 1, Feb. 2000) for a more detailed discussion of the written description requirement and its relationship to new matter.

[17] The claims as filed in the original specification are part of the disclosure and, therefore, if an application as originally filed contains a claim disclosing material not found in the remainder of the specification, the applicant may amend the specification to include the claimed subject matter. *In re Benno*, 768 F.2d 1340, 226 USPQ 683 (Fed. Cir. 1985).

[18] *See, e.g., In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads).

[19] *In re Oda*, 443 F.2d 1200, 170 USPQ 260 (CCPA 1971). With respect to the correction of sequencing errors in applications disclosing nucleic acid and/or amino acid sequences, it is well known that sequencing errors are a common problem in molecular biology. *See, e.g.*, Peter Richterich, *Estimation of Errors in 'Raw' DNA Sequences: A Validation Study*, 8 Genome Research 251–59 (1998). If an application as filed includes sequence information and references a deposit of the sequenced material made in accordance with the requirements of 37 CFR § 1.801 *et seq.*, amendment may be permissible.

[20] Corrections of minor errors in the sequence may be possible based on the argument that one of skill in the art would have resequenced the deposited material and would have immediately recognized the minor error. Deposits made after the filing date can only be relied upon to provide support for the correction of sequence information if applicant submits a statement in compliance with 37 CFR § 1.804 stating that the biological material which is deposited is a biological material specifically defined in the application as filed.

[21] *See, e.g., Gentry Gallery, Inc.* v. *Berkline Corp.*, 134 F.3d 1473, 45 USPQ2d 1498 (Fed. Cir. 1998) (claims to a sectional sofa comprising, *inter alia*, a console and a control means were held invalid for failing to satisfy the written description requirement where the claims were broadened by removing the location of the control means.); *Johnson Worldwide Associates* v. *Zebco Corp.*, 175 F.3d 985, 993, 50 USPQ2d 1607, 1613 (Fed. Cir. 1999) (In *Gentry Gallery*, the "court's determination that the patent disclosure did not support a broad meaning for the disputed claim terms was premised on clear statements in the written description that described the location of a claim element—the 'control means'—as 'the only possible location' and that variations were 'outside the stated purpose of the invention.' *Gentry Gallery*, 134 F.3d at 1479, 45 USPQ2d at 1503. *Gentry Gallery*, then, considers the situation where the patent's disclosure makes crystal clear that a particular (*i.e.*, narrow) understanding of a claim term is an 'essential element of [the inventor's] invention.'"); *Tronzo* v. *Biomet*, 156 F.3d at 1158–59, 47 USPQ2d at 1833 (Fed. Cir. 1998) (claims to generic cup shape were not entitled to filing date of parent application which disclosed "conical cup" in view of the disclosure of the

parent application stating the advantages and importance of the conical shape.).

[22] *See Gentry Gallery*, 134 F.3d at 1480, 45 USPQ2d at 1503; *In re Sus*, 306 F.2d 494, 504, 134 USPQ 301, 309 (CCPA 1962) ("[O]ne skilled in this art would not be taught by the written description of the invention in the specification that any 'aryl or substituted aryl radical' would be suitable for the purposes of the invention but rather that only *certain aryl radicals* and certain specifically substituted aryl radicals [*i.e.*, aryl azides] would be suitable for such purposes.") (emphasis in original). A claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may also be subject to rejection under 35 U.S.C. 112, ¶ 1, as not enabling, or under 35 U.S.C. 112, ¶ 2. *See In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976); and *In re Collier*, 397 F.2d 1003, 158 USPQ 266 (CCPA 1968). *See also* MPEP § 2172.01.

[23] *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563–64, 19 USPQ2d at 1117.

[24] *Wertheim*, 541 F.2d at 262, 191 USPQ at 96.

[25] *See* MPEP §§ 714.02 and 2163.06 ("Applicant should * * * specifically point out the support for any amendments made to the disclosure."); and MPEP § 2163.04 ("If applicant amends the claims and points out where and/or how the originally filed disclosure supports the amendment(s), and the examiner finds that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of the filing of the application, the examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.").

[26] *See In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ("Precisely how close [to the claimed invention] the description must come to comply with § 112 must be left to case-by-case development."); *In re Wertheim*, 541 F.2d at 262, 191 USPQ at 96 (inquiry is primarily factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure).

[27] *See, e.g., In re Morris*, 127 F.3d 1048, 1053–54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).

[28] "Preamble language" is that language in a claim appearing before the transitional phase, *e.g.*, before "comprising," "consisting essentially of," or "consisting of."

[29] The transitional term "comprising" (and other comparable terms, *e.g.*, "containing," "including," and "having") is "open-ended—it covers the expressly recited subject matter, alone or in combination with unrecited subject matter. *See, e.g., Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim."); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves the "claim open for the inclusion of unspecified ingredients even in major amounts"). "By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format." *PPG Industries v. Guardian Industries*, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353–54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to "comprising." *See, e.g., PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase "consisting essentially of" for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). *See also In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895–96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964).

[30] *See Pac-Tec Inc. v. Amerace Corp.*, 903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention).

[31] An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

[32] *See, e.g., Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995) ("[A] claim preamble has the import that the claim as a whole suggests for it."); *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989) (The determination of whether preamble recitations are structural limitations can be resolved only on review of the entirety of the application "to gain an understanding of what the inventors actually invented and intended to encompass by the claim.").

[33] An element may be critical where those of skill in the art would require it to determine that applicant was in possession of the invention. *Compare Rasmussen*, 650 F.2d at 1215, 211 USPQ at 327 ("one skilled in the art who read Rasmussen's specification would understand that it is unimportant *how* the layers are adhered, so long as they are adhered") (emphasis in original), *with Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) ("it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it").

[34] *See, e.g., Wang Labs. v. Toshiba Corp.*, 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993).

[35] *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379–80, 231 USPQ 81, 90 (Fed. Cir. 1986).

[36] *See, e.g., Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, ___, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) (the written description "inquiry is a factual one and must be assessed on a case-by-case basis"); *see also Pfaff v. Wells Electronics, Inc.*, 55 U.S. at 66, 119 S.Ct. at 311, 48 USPQ2d at 1646 ("The word 'invention' must refer to a concept that is complete, rather than merely one that is 'substantially complete.' It is true that reduction to practice ordinarily provides the best evidence that an invention is complete. But just because reduction to practice is sufficient evidence of completion, it does not follow that proof of reduction to practice is necessary in every case. Indeed, both the facts of the *Telephone Cases* and the facts of this case demonstrate that one can prove that an invention is complete and ready for patenting before it has actually been reduced to practice.").

[37] *Cooper v. Goldfarb*, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). *See also UMC Elecs. Co. v. United States*, 816 F.2d 647, 652, 2 USPQ2d 1465, 1468 (Fed. Cir. 1987) ("[T]here cannot be a reduction to practice of the invention * * * without a physical embodiment which includes all limitations of the claim."); *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 593, 44 USPQ2d 1610, 1614 (Fed. Cir. 1997) ("[A] reduction to practice does not occur until the inventor has determined that the invention will work for its intended purpose."); *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1578, 38 USPQ2d 1288, 1291 (Fed. Cir. 1996) (determining that the invention will work for its intended purpose may require testing depending on the character of the invention and the problem it solves).

[38] 37 CFR 1.804, 1.809. *See also* endnote 6.

[39] *See, e.g., Vas-Cath*, 935 F.2d at 1565, 19 USPQ2d at 1118 ("drawings alone may provide a 'written description' of an invention as required by § 112"); *In re Wolfensperger*, 302 F.2d 950, 133 USPQ 537 (CCPA 1962) (the drawings of applicant's specification provided sufficient written descriptive support for the claim limitation at issue); *Autogiro Co. of America v. United States*, 384 F.2d 391, 398, 155 USPQ 697, 703 (Ct. Cl. 1967) ("In those instances where a visual representation can flesh out words, drawings may be used in the same manner and with the same limitations as the specification.").

[40] *See, e.g., Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.").

[41] *See Hybritech* v. *Monoclonal Antibodies*, 802 F.2d at 1384, 231 USPQ at 94; *Fonar Corp.* v. *General Electric Co.*, 107 F.3d at 1549, 41 USPQ2d at 1805 (source code description not required).

[42] For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been isolated. One skilled in the art may be able to determine when the gene disclosed is the same as or different from a gene isolated by another by comparing the restriction enzyme map. In contrast, evidence that the gene could be digested with a nuclease would not normally represent a relevant characteristic since any gene would be digested with a nuclease. Similarly, isolation of an mRNA and its expression to produce the protein of interest is strong evidence of possession of an mRNA for the protein.

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention").

[43] A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. *See also Fiers*, 984 F.2d at 1169–71, 25 USPQ2d at 1605–06 (discussing *Amgen Inc.* v. *Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)).

[44] If a claim limitation invokes 35 U.S.C. 112, ¶ 6, it must be interpreted to cover the corresponding structure, materials, or acts in the specification and "equivalents thereof." *See* 35 U.S.C. 112, ¶ 6. *See also B. Braun Medical, Inc.* v. *Abbott Lab.*, 124 F.3d 1419, 1424, 43 USPQ2d 1896, 1899 (Fed. Cir. 1997). In considering whether there is 35 U.S.C. 112, ¶ 1, support for a means- (or step) plus-function claim limitation, the examiner must consider not only the original disclosure contained in the summary and detailed description of the invention portions of the specification, but also the original claims, abstract, and drawings. A means- (or step-) plus-function claim limitation is adequately described under 35 U.S.C. 112, ¶ 1, if: (1) The written description adequately links or associates adequately described particular structure, material, or acts to the function recited in a means- (or step-) plus-function claim limitation; or (2) it is clear based on the facts of the application that one skilled in the art would have known what structure, material, or acts perform the function recited in a means- (or step-) plus-function limitation. Note also: A rejection under 35 U.S.C. 112, ¶ 2, "cannot stand where there is adequate description in the specification to satisfy 35 U.S.C. 112, first paragraph, regarding means-plus-function recitations that are not, per se, challenged for being unclear." *In re Noll*, 545 F.2d 141, 149, 191 USPQ 721, 727 (CCPA 1976). *See Supplemental Examination Guidelines for Determining the Applicability of 35 U.S.C. 112, ¶ 6*, 65 FR 38510, June 21, 2000.

[45] *See Hybritech Inc.* v. *Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94.

[46] *See, e.g., Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin* v. *Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [*i.e.*, "in the same words"] to be sufficient").

[47] A claim which is limited to a single disclosed embodiment or species is analyzed as a claim drawn to a single embodiment or species, whereas a claim which encompasses two or more embodiments or species within the scope of the claim is analyzed as a claim drawn to a genus. *See also* MPEP § 806.04(e).

[48] 35 U.S.C. 112, ¶ 1. *Cf. Fields* v. *Conover*, 443 F.2d 1386, 1392, 170 USPQ 276, 280 (CCPA 1971) (finding a lack of written description because the specification lacked the "full, clear, concise, and exact written description" which is necessary to support the claimed invention).

[49] For example, if the art has established a strong correlation between structure and function, one skilled in the art would be able to predict with a reasonable degree of confidence the structure of the claimed invention from a recitation of its function. Thus, the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. In contrast, without such a correlation, the capability to recognize or understand the structure from the mere recitation of function and minimal structure is highly unlikely. In this latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372–73 (Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). *Compare Fonar*, 107 F.3d at 1549, 41 USPQ2d at 1805 (disclosure of software function adequate in that art).

[50] *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

[51] *See, e.g., In re Hayes Microcomputer Products, Inc. Patent Litigation*, 982 F.2d 1527, 1534–35, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992) ("One skilled in the art would know how to program a microprocessor to perform the necessary steps described in the specification. Thus, an inventor is not required to describe every detail of his invention. An applicant's disclosure obligation varies according to the art to which the invention pertains. Disclosing a microprocessor capable of performing certain functions is sufficient to satisfy the requirement of section 112, first paragraph, when one skilled in the relevant art would understand what is intended and know how to carry it out.")

[52] *See, e.g., Fiers* v. *Revel*, 984 F.2d at 1169, 25 USPQ2d at 1605; *Amgen.*, 927 F.2d at 1206, 18 USPQ2d at1021. Where the process has actually been used to produce the product, the written description requirement for a product-by-process claim is clearly satisfied; however, the requirement may not be satisfied where it is not clear that the acts set forth in the specification can be performed, or that the product is produced by that process.

[53] *See, e.g., Amgen*, 927 F.2d at1206, 18 USPQ2d at 1021 ("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated.") (citations omitted). In such instances the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor's idea of the invention. *Burroughs Wellcome Co.* v. *Barr Laboratories Inc.*, 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention. *Id.*

[54] *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

[55] *See, e.g., Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326–27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteriod in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary

to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."); *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973) (the phrase "air or other gas which is inert to the liquid" was sufficient to support a claim to "inert fluid media" because the description of the properties and functions of the air or other gas segmentizing medium would suggest to a person skilled in the art that appellant's invention includes the use of "inert fluid" broadly.). However, in *Tronzo v. Biomet*, 156 F.3d at 1159, 47 USPQ2d at1833 (Fed. Cir. 1998), the disclosure of a species in the parent application did not suffice to provide written description support for the genus in the child application.

[56] *See, e.g., Eli Lilly.*

[57] For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species. *Cf. In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

[58] *See Wertheim*, 541 F.2d at 263, 191 USPQ at 97 ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.").

[59] *See* MPEP §§ 714.02 and 2163.06 ("Applicant should * * * specifically point out the support for any amendments made to the disclosure.").

[60] *See, e.g., In re Wright*, 866 F.2d 422, 425, 9 USPQ2d 1649, 1651 (Fed. Cir. 1989) (Original specification for method of forming images using photosensitive microcapsules which describes removal of microcapsules from surface and warns that capsules not be disturbed prior to formation of image, unequivocally teaches absence of permanently fixed microcapsules and supports amended language of claims requiring that microcapsules be "not permanently fixed" to underlying surface, and therefore meets description requirement of 35 U.S.C. 112.).

[61] *See, e.g., In re Robins*, 429 F.2d 452, 456–57, 166 USPQ 552, 555 (CCPA 1970) ("[W]here no explicit description of a generic invention is to be found in the specification * * * mention of representative compounds may provide an implicit description upon which to base generic claim language."); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily implicitly described by a genus encompassing it and a species upon which it reads).

[62] *See, e.g., In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950–51 (Fed. Cir. 1999) ("To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.""") (citations omitted).

[63] When an explicit limitation in a claim "is not present in the written description whose benefit is sought it must be shown that a person of ordinary skill would have understood, at the time the patent application was filed, that the description requires that limitation." *Hyatt v. Boone*, 146 F.3d 1348, 1353, 47 USPQ2d 1128, 1131 (Fed. Cir. 1998).

[64] *See, e.g., Johnson Worldwide Associates Inc. v. Zebco Corp.*, 175 F.3d at 993, 50 USPQ2d at 1613; *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d at 1479, 45 USPQ2d at 1503; *Tronzo v. Biomet*, 156 F.3d at 1159, 47 USPQ2d at 1833.

[65] *See, e.g., In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

[66] *Wertheim*, 541 F.2d at 263, 191 USPQ at 97.

[67] *See Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326.

[68] *See In re Alton*, 76 F.3d 1168, 1176, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

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CORPORATION FOR NATIONAL AND COMMUNITY SERVICE

Revision of Currently Approved Information Collection; Comment Request

AGENCY: Corporation for National and Community Service

ACTION: Notice.

SUMMARY: The Corporation for National and Community Service (hereinafter "Corporation"), as part of its continuing effort to reduce paperwork and respondent burden, conducts a preclearance consultation program to provide the general public and Federal agencies with an opportunity to comment on proposed and/or continuing collections of information in accordance with the Paperwork Reduction Act of 1995 (PRA95) (44 U.S.C. 3506(c)(2)(A)). This program helps to ensure that requested data can be provided in the desired format, reporting burden (time and financial resources) is minimized, collection instruments are clearly understood, and the impact of collection requirement on respondents can be properly assessed.

Currently, the Corporation is soliciting comments concerning the proposed revision of its Voucher and Payment Request Form (OMB #3045–0014).

Copies of the forms can be obtained by contacting the office listed below in the address section of this notice.

DATES: Written comments must be submitted to the office listed in the **ADDRESSES** section by March 6, 2001.

ADDRESSES: Send comments to Levon Buller, National Service Trust, Corporation for National and Community Service, 1201 New York Ave., NW., Washington, DC 20525.

FOR FURTHER INFORMATION CONTACT: Levon Buller, (202) 606–5000, ext. 383.

SUPPLEMENTARY INFORMATION: The Corporation is particularly interested in comments which:

- Evaluate whether the proposed collection of information is necessary for the proper performance of the functions of the Corporation, including whether the information will have practical utility;
- Evaluate the accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used;
- Enhance the quality, utility and clarity of the information to be collected; and
- Minimize the burden of the collection of information on those who are to respond, including through the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology, *e.g.*, permitting electronic submissions of responses.

Background

The Corporation supports programs that provide opportunities for individuals who want to become involved in national service. The service opportunities cover a wide range of activities over varying periods of time. Upon successfully completing an agreed-upon term of service in an approved AmeriCorps program, a national service participant—an AmeriCorps member—receives an "education award". This award is an amount of money set aside in the member's name in the National Service Trust Fund. This education award can be used to make payments towards qualified student loan or pay for educational expenses at qualified post-secondary institutions and approved school-to-work opportunities programs. Members have seven years in which to draw against any unused balance.

The National Service Trust is the office within the Corporation that administers the education award

Appendix E
Press Release #00-15, USPTO
March 1, 2000

PRESS RELEASE #00-15
March 1, 2000

CONTACT: **Brigid Quinn**
703-305-8341

PTO OFFERS TRAINING MATERIALS FOR INTERIM WRITTEN DESCRIPTION AND UTILITY GUIDELINES

The Patent and Trademark Office (PTO) today posted training materials designed to aid PTO's patent examiners in applying the interim written description and utility guidelines in a uniform and consistent manner to promote the issuance of high quality patents. The training materials will also assist patent applicants in responding to the PTO when utility or written description issues are raised during the examination of a patent application. The training materials can be found at http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf and http://www.uspto.gov/web/offices/pac/writtendesc.pdf. The guidelines were published in the Federal Register on December 21, 1999.

"I was very pleased with the breadth and the depth of the public comments that helped us shape our interim written description and utility guidelines," noted Q. Todd Dickinson, Commissioner of Patents and Trademarks. "I expect that the training materials we posted today will further inform the debate, supporting our efforts to strike the right balance with the final guidelines."

The Written Description training materials contain examples that are applicable to all areas of technology and all types of inventions. The examples include a variety of fact patterns and associated claims and conclude with a detailed claims analysis and recommended legal conclusions. Examples are provided in the mechanical, electrical, and biotechnological arts, and are based both on recent court decisions and typically encountered fact-patterns. The training materials emphasize that compliance with the written description requirement will be determined on a case-by-case basis. These materials serve to guide the examiners in determining whether the inventor has provided the necessary description of the invention.

The revised Interim Utility training materials focus on a three-pronged test for determining whether or not an invention is "useful" within the meaning of the law: Does the invention have a utility that is specific, substantial and credible? The materials include definitions of the elements that make up this test. A specific utility is one that is particular to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention.

A substantial utility is one that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A utility is credible unless the logic underlying the assertion is seriously flawed, or the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. All of the examples in the utility training materials are in the biotechnology or chemical arts.

The period for public comment on the revised Utility guidelines and the revised Interim Written Description guidelines continues until March 22, 2000, and all such comments are welcome.

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